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2600 MCQ with Illustrated Answer
Full Topics Note
14 Chapter

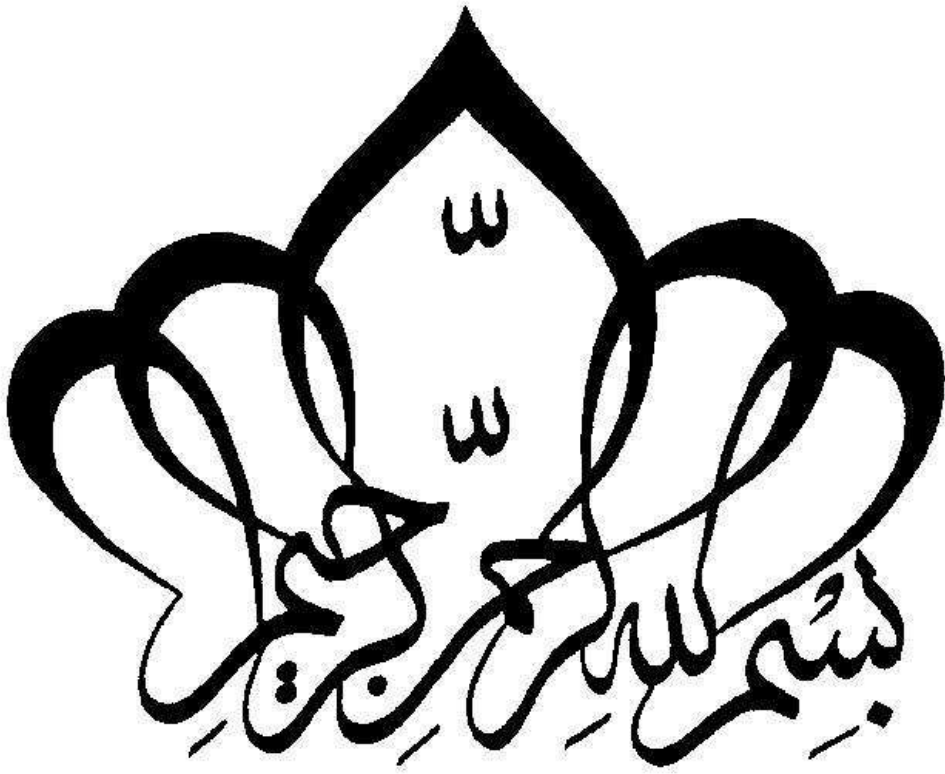
Endocrinology

P. M MCQ Bank 2017



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قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
۞ إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

إهداء

للكل آية من كتاب الله حفظناها ولكل معلومة قرأناها ونسيناها لعل الله يحمينا من النسيان ويروها إلينا
للكل شخص وعونا له في ظهر الغيب لعل الله أن يستجيب دعائنا
للكل مريض قرأ له ما أله لعل الله يشفيه ويعير إليه صحته وعافيته
للكل لحظة تألم بها أحببنا لعل الله لا يريهم الألم ولا يضييهم مرة أخرى
للكل موقف اجتجت به عيناى فلم تلبيانى لعل الله لا يضرنى بهما في حياتى
للكل حالم صاحب أهراء ومباوى لعل الله يحقق له مقاصده حتى يرضيه ويرضى عنه
للكل مجتهد لعل الله يجعل له من التوفيق أوفر حظ ونصيب ويهون له الأسباب كلها من حيث لا يدري من غير ضراء مضرة ولا فتنة مضلة
للكل من فقر شيئا في الحياة لعل الله يعيره إليه أو يعوضه بما يسعده
للكل شخص ابتعدنا عنه لعل الله يجمعه بمن هم أفضل منا
وأخيرا وليس آخرا لأهلنا لعل الله يجعلها لهم صرقة جارية ترو إليهم قليلا من فضلهم علينا وتكون سببا يلم شملنا تحت سقف واحد بعد أن
هجرتنا الحروب والمصائب

يقول أحد الصالحين

إِذَا رَأَيْتَ أَنَّ اللَّهَ وَفَقَكَ لِإِخْوَةِ تَعْيْنِكَ عَلَى الْخَيْرِ.. فَأَعْلَمْ أَنَّ اللَّهَ يَرِيدُ بِكَ خَيْرًا !! وَإِذَا وَفَقَكَ اللَّهَ لِلدُّعَاءِ.. فَأَعْلَمْ أَنَّ اللَّهَ يَرِيدُ أَنْ يُعْطِيَكَ !! وَإِذَا
وَفَقَكَ لِقَضَاءِ حَوَائِجِ النَّاسِ فَأَعْلَمْ أَنَّ لَكَ يَتَخَلَّى عَنْكَ !! وَإِذَا وَفَقَكَ اللَّهَ لِذِكْرِهِ.. فَأَعْلَمْ أَنَّكَ مُحِبٌّ !!.. وَإِذَا أَحْبَبَّكَ أَحَدٌ.. وَنَصَرَكَ.. وَأَيَّرَكَ..
وَأُسْتَجَابَ لِدُعَائِكَ !!

This issue of **MRCPPART1 MADE EASY 2017** contains the following:

- Full topic note.
- Around 2600 MCQs from **PM 2017 BANK** covering 14 chapter in internal medicine
- External links for the related guidelines (such as NICE, SIGN, RCP ...etc).
- Comments with illustrative pictures and links to external media.
- Most Recommended QBank for MRCP Part 1, Arab Board, Jordanian Board and other internal medicine assessment exams.

Please Note that

Each chapter begins with notes section. These notes are repeated under the Questions in the website. In these collections the notes are not repeated under each question except in some to avoid unnecessary repetition. For clarity and convenience the title of the related note is only mentioned after the comments in case the reader want to refer back to the respective note in the notes section.

The illustration below is to show and Example

☐	Minimal change disease
☐	Post-streptococcal glomerulonephritis
☐	Goodpasture's syndrome

Goodpasture's syndrome

- IgG deposits on renal biopsy
- anti-GBM antibodies

• These changes are characteristic of Goodpasture's syndrome.

[Discuss and give feedback](#)

Goodpasture's syndrome 

Comment of the Q

title of the note in case the reader want to refer back to the notes sections

MRCPPART1 MADE EASY 2017

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إعداد وتنسيق

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&

A. MURAD

لا تنسونا من صالح دعائكم

ما كان من خطأ فمن أنفسنا وما كان من توفيق فمن الله

تم بحمد الله وتوفيقه ومنه

جعل الله عملنا متقبلاً خالصاً لوجهه الكريم

Reference ranges

Reference ranges vary according to individual labs. All values are for adults unless otherwise stated

Full blood count

Haemoglobin	Men: 13.5-18 g/dl Women: 11.5-16 g/dl
Mean cell volume	82-100 fl
Platelets	150-400 * 10 ⁹ /l
White blood cells	4-11 * 10 ⁹ /l

Urea and electrolytes

Sodium	135-145 mmol/l
Potassium	3.5 - 5.0 mmol/l
Urea	2.0-7 mmol/l
Creatinine	55-120 umol/l
Bicarbonate	22-28 mmol/l
Chloride	95-105 mmol/l

Liver function tests

Bilirubin	3-17 umol/l
Alanine transferase (ALT)	3-40 iu/l
Aspartate transaminase (AST)	3-30 iu/l
Alkaline phosphatase (ALP)	30-100 umol/l
Gamma glutamyl transferase (yGT)	8-60 u/l
Albumin	35-50 g/l
Total protein	60-80 g/l

Other haematology

Erythrocyte sedimentation rate (ESR)	Men: < (age / 2) mm/hr Women: < ((age + 10) / 2) mm/hr
Prothrombin time (PT)	10-14 secs
Activated partial thromboplastin time (APTT)	25-35 secs
Ferritin	20-230 ng/ml
Vitamin B12	200-900 ng/l
Folate	3.0 nmol/l
Reticulocytes	0.5-1.5%
D-Dimer	< 400 ng/ml

Other biochemistry

Calcium	2.1-2.6 mmol/l
Phosphate	0.8-1.4 mmol/l
CRP	< 10 mg/l
Thyroid stimulating hormone (TSH)	0.5-5.5 mu/l
Free thyroxine (T4)	9-18 pmol/l
Total thyroxine (T4)	70-140 nmol/l
Amylase	70-300 u/l

Uric acid	0.18-0.48 mmol/l
-----------	------------------

Arterial blood gases

pH	7.35 - 7.45
pCO2	4.5 - 6.0 kPa
pO2	10 - 14 kPa

Lipids

Desirable lipid values depend on other risk factors for cardiovascular disease, below is just a guide:

Total cholesterol	< 5 mmol/l
Triglycerides	< 2 mmol/l
HDL cholesterol	> 1 mmol/l
LDL cholesterol	< 3 mmol/l

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Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

Features

- coarse facial appearance, spade-like hands, increase in shoe size
- large tongue, prognathism, interdental spaces
- excessive sweating and oily skin
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases → galactorrhoea
- 6% of patients have MEN-1

Complications

- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

Acromegaly: investigations

◆Growth hormone (GH) levels vary during the day and are therefore not diagnostic. The definitive test is the oral glucose tolerance (OGTT) with serial GH measurements. Serum IGF-1 may also be used as a screening test and is sometimes used to monitor disease

Oral glucose tolerance test

- in normal patients GH is suppressed to < 2 mu/L with hyperglycaemia
- in acromegaly there is no suppression of GH
- may also demonstrate impaired glucose tolerance which is associated with acromegaly

A pituitary MRI may demonstrate a pituitary tumour

Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients.

Dopamine agonists

- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue

- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant

- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment

External Links

[Postgraduate Medical Journal](#)

Modern treatment of acromegaly

Addison's disease

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

Features

- lethargy, weakness, anorexia, nausea & vomiting, weight loss, 'salt-craving'
- hyperpigmentation (especially palmar creases), vitiligo, loss of pubic hair in women, hypotension
- crisis: collapse, shock, pyrexia

Other causes of hypoadrenalism

Primary causes

- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)
- HIV
- antiphospholipid syndrome

Secondary causes

- pituitary disorders (e.g. tumours, irradiation, infiltration)

Exogenous glucocorticoid therapy

External Link

[Postgraduate Medical Journal](#)

Review of endocrine emergencies

Addison's disease: investigations

In a patient with suspected Addison's disease the definite investigation is a ACTH stimulation test (short Synacthen test). Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated.

If a ACTH stimulation test is not readily available (e.g. in primary care) then sending a 9 am serum cortisol can be useful:

- > 500 nmol/l makes Addison's very unlikely
- < 100 nmol/l is definitely abnormal
- 100-500 nmol/l should prompt a ACTH stimulation test to be performed

Associated electrolyte abnormalities are seen in around one-third of undiagnosed patients:

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

Addisonian crisis

Causes

- sepsis or surgery causing an acute exacerbation of chronic insufficiency (Addison's, Hypopituitarism)
- adrenal haemorrhage eg Waterhouse-Friderichsen syndrome (fulminant meningococemia)
- steroid withdrawal

Management

- hydrocortisone 100 mg im or iv
- 1 litre normal saline infused over 30-60 mins or with dextrose if hypoglycaemic
- continue hydrocortisone 6 hourly until the patient is stable. No fludrocortisone is required because high cortisol exerts weak mineralocorticoid action.
- oral replacement may begin after 24 hours and be reduced to maintenance over 3-4 days.

Amenorrhoea

Amenorrhoea may be divided into primary (failure to start menses by the age of 16 years) or secondary (cessation of established, regular menstruation for 6 months or longer).

Causes of primary amenorrhoea:

- Turner's syndrome
- testicular feminisation
- congenital adrenal hyperplasia
- congenital malformations of the genital tract

Secondary amenorrhoea is defined as when menstruation has previously occurred but has now stopped for at least 6 months.

Causes of secondary amenorrhoea (after excluding pregnancy):

- hypothalamic amenorrhoea (e.g. Stress, excessive exercise)
- polycystic ovarian syndrome (PCOS)
- hyperprolactinaemia
- premature ovarian failure
- thyrotoxicosis*
- Sheehan's syndrome
- Asherman's syndrome (intrauterine adhesions)

Initial investigations

- exclude pregnancy with urinary or serum bHCG
- gonadotrophins: low levels indicate a hypothalamic cause where as raised levels suggest an ovarian problem (e.g. Premature ovarian failure)
- prolactin
- androgen levels: raised levels may be seen in PCOS
- oestradiol
- thyroid function tests
*hypothyroidism may also cause amenorrhoea

Androgen insensitivity syndrome

Androgen insensitivity syndrome is an X-linked recessive condition due to end-organ resistance to testosterone causing genotypically male children (46XY) to have a female phenotype. Complete androgen insensitivity syndrome is the new term for testicular feminisation syndrome.

Features

- 'primary amenorrhoea'
- undescended testes causing groin swellings
- breast development may occur as a result of conversion of testosterone to oestradiol

Diagnosis

- buccal smear or chromosomal analysis to reveal 46XY genotype

Management

- counselling - raise child as female
- bilateral orchidectomy (increased risk of testicular cancer due to undescended testes)
- oestrogen therapy

Apparent mineralocorticoid excess

◆In order to prevent cortisol activation of the mineralocorticoid nuclear receptor and subsequent hyperaldosteronism, 11-hydroxysteroid dehydrogenase type 2 converts cortisol into inactive cortisone at the renal parenchyma.

◆**Apparent mineralocorticoid excess (AME)** is often inherited, caused by an autosomal recessive mutation in 11-hydroxysteroid dehydrogenase type 2. However rarely excess liquorice can cause inhibition of 11-hydroxysteroid dehydrogenase type 2 leading to excess cortisol and thus AME.

◆Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

♦APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. **Patients have Addison's disease plus either:**

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed):

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types

Bartter's syndrome

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the $\text{Na}^+ \text{K}^+ 2\text{Cl}^-$ cotransporter (NKCC2) in the ascending loop of Henle. It should be noted that it is associated with normotension (unlike other endocrine causes of hypokalaemia such as Conn's, Cushing's and Liddle's syndrome which are associated with hypertension).

♦Loop diuretics work by inhibiting NKCC2 - think of Bartter's syndrome as like taking large doses of furosemide

Features

- usually presents in childhood, e.g. Failure to thrive
- polyuria, polydipsia
- hypokalaemia
- normotension
- weakness

External Links

[Royal College of Physicians](#)

2012 Renal tubular disorders review

Carbimazole

♦ Carbimazole is used in the management of thyrotoxicosis. It is typically given in high doses for 6 weeks until the patient becomes euthyroid before being reduced.

Mechanism of action

- blocks thyroid peroxidase from coupling and iodinating the tyrosine residues on thyroglobulin → reducing thyroid hormone production
- in contrast propylthiouracil as well as this central mechanism of action also has a peripheral action by inhibiting 5'-deiodinase which reduces peripheral conversion of T4 to T3

Adverse effects

- agranulocytosis
- crosses the placenta, but may be used in low doses during pregnancy

External Links

Carcinoid tumours

Carcinoid syndrome

- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

Features

- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

Investigation

- urinary 5-HIAA
- plasma chromogranin A y

Management

- somatostatin analogues e.g. octreotide
 - diarrhoea: cyproheptadine may help
-

Congenital adrenal hyperplasia: features

21-hydroxylase deficiency features:

- virilisation of female genitalia
- precocious puberty in males
- 60-70% of patients have a salt-losing crisis at 1-3 wks of age

11-beta hydroxylase deficiency features:

- virilisation of female genitalia
- precocious puberty in males
- hypertension
- hypokalaemia

17-hydroxylase deficiency features:

- non-virilising in females
- inter-sex in boys
- hypertension

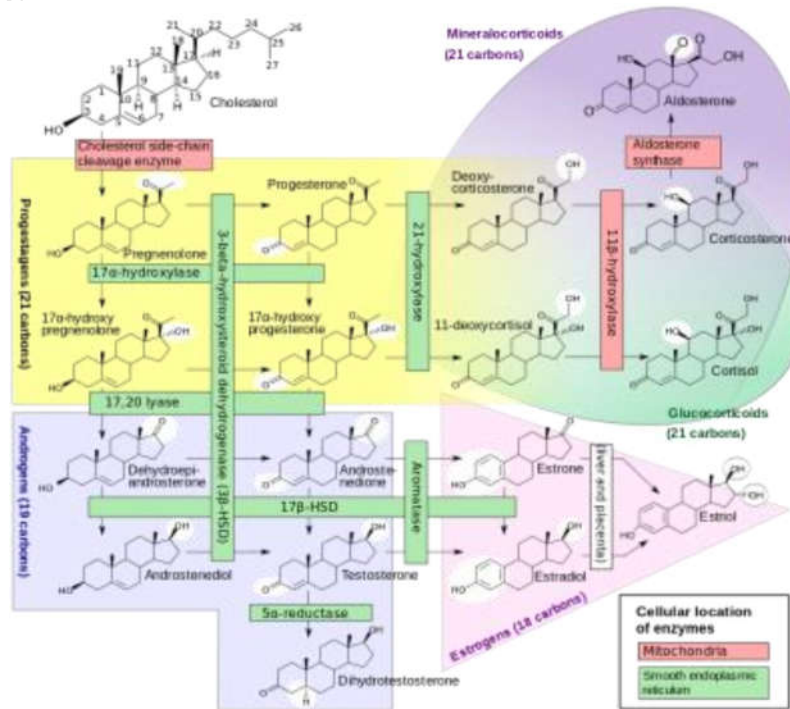


Image sourced from [Wikipedia](#)

Congenital hypothyroidism

Congenital hypothyroidism affects around 1 in 4000 babies. If not diagnosed and treated within the first four weeks it causes irreversible cognitive impairment

Features

- prolonged neonatal jaundice
- delayed mental & physical milestones
- short stature
- puffy face, macroglossia
- hypotonia

Children are screened at 5-7 days using the heel prick test

Corticosteroids

Corticosteroids are amongst the most commonly prescribed therapies in clinical practice. They are used both systemically (oral or intravenous) or locally (skin creams, inhalers, eye drops, intra-articular). They augment and in some cases replace the natural glucocorticoid and mineralocorticoid activity of endogenous steroids.

The relative glucocorticoid and mineralocorticoid activity of commonly used steroids is shown below:

Minimal glucocorticoid activity, very high mineralocorticoid activity,	Glucocorticoid activity, high mineralocorticoid activity,	Predominant glucocorticoid activity, low mineralocorticoid activity	Very high glucocorticoid activity, minimal mineralocorticoid activity
Fludrocortisone	Hydrocortisone	Prednisolone	Dexamethasone Betmethasone

Side-effects

The side-effects of corticosteroids are numerous and represent the single greatest limitation on their usage. Side-effects are more common with systemic and prolonged therapy.

Glucocorticoid side-effects

- endocrine: impaired glucose regulation, increased appetite/weight gain, hirsutism, hyperlipidaemia
- Cushing's syndrome: moon face, buffalo hump, striae
- musculoskeletal: osteoporosis, proximal myopathy, avascular necrosis of the femoral head
- immunosuppression: increased susceptibility to severe infection, reactivation of tuberculosis
- psychiatric: insomnia, mania, depression, psychosis
- gastrointestinal: peptic ulceration, acute pancreatitis
- ophthalmic: glaucoma, cataracts
- suppression of growth in children
- intracranial hypertension

Mineralocorticoid side-effects

- fluid retention
- hypertension

Selected points on the use of corticosteroids:

- patients on long-term steroids should have their doses doubled during intercurrent illness
- the BNF suggests gradual withdrawal of systemic corticosteroids if patients have: received more than 40mg prednisolone daily for more than one week, received more than 3 weeks treatment or recently received repeated courses

Cushing's syndrome: causes

ACTH dependent causes:

- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes:

- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's:

- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

External Links

[DermNet NZ](#)

Side-effects of systemic steroids.

Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test

- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation

- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

Diabetes mellitus (type 2): diagnosis

The diagnosis of type 2 diabetes mellitus can be made by either a plasma glucose or a HbA1c sample. Diagnostic criteria vary according to whether the patient is symptomatic (polyuria, polydipsia etc) or not.

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

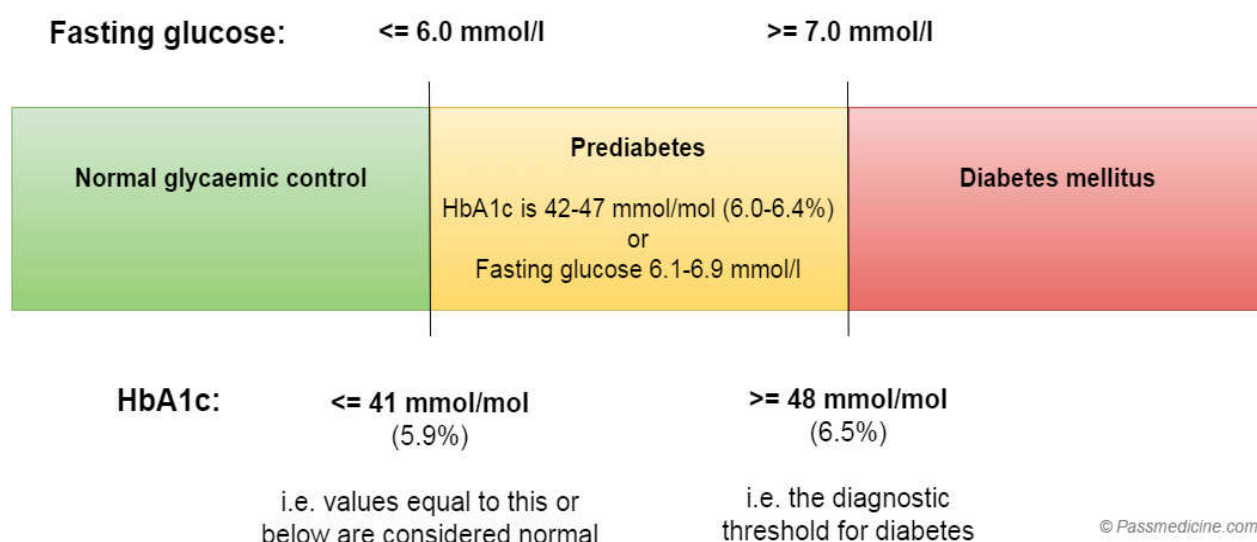


Diagram showing the spectrum of diabetes diagnosis

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 48 mmol/mol (6.5%) is diagnostic of diabetes mellitus
- a HbA1c value of less than 48 mmol/mol (6.5%) does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (see below).

Conditions where HbA1c may not be used for diagnosis:

- haemoglobinopathies
- haemolytic anaemia
- untreated iron deficiency anaemia
- suspected gestational diabetes
- children
- HIV
- chronic kidney disease

Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

External Links

[WHO](#)

2006 guidelines

[WHO](#)

Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus

[Diabetes UK](#)

New diagnostic criteria for diabetes

[NICE](#)

2015 Type 2 diabetes mellitus guidelines

Diabetes mellitus: a very basic introduction

Diabetes mellitus is one of the most common conditions encountered in clinical practice and represents a significant burden on the health systems of the developed world. It is now estimated that 8% of the total NHS budget is now spent on managing patients with diabetes mellitus.

What is diabetes mellitus?

Diabetes mellitus may be defined as a chronic condition characterised by abnormally raised levels of blood glucose.

Why is the management of diabetes mellitus so important?

Before the advent of insulin therapy untreated type 1 diabetes would usually result in death. Poorly treated type 1 diabetes mellitus can still result in significant morbidity and mortality (as a result of diabetic ketoacidosis). However, the main focus of diabetes management now is reducing the incidence of macrovascular (ischaemic heart disease, stroke) and microvascular (eye, nerve and kidney damage) complications.

Types of diabetes mellitus

There are a number of different types of diabetes mellitus:

Type	Notes
Type 1 diabetes mellitus (T1DM)	Autoimmune disorder where the insulin-producing beta cells of the islets of Langerhans in the pancreas are destroyed by the immune system This results in an absolute deficiency of insulin resulting in raised glucose levels Patients tend to develop T1DM in childhood/early adult life and typically present unwell, possibly in diabetic ketoacidosis
Type 2 diabetes mellitus (T2DM)	This is the most common cause of diabetes in the developed world. It is caused by a relative deficiency of insulin due to an excess of adipose tissue. In simple terms there isn't enough insulin to 'go around' all the excess fatty tissue, leading to blood glucose creeping up.
Prediabetes	This term is used for patients who don't yet meet the criteria for a formal diagnosis of T2DM to be made but are likely to develop the condition over the next few years. They, therefore, require closer monitoring and lifestyle interventions such as weight loss
Gestational diabetes	Some pregnant develop raised glucose levels during pregnancy. This is important to detect as untreated it may lead to adverse outcomes for the mother and baby
Maturity onset diabetes of the	A group of inherited genetic disorders affecting the production of insulin. Results in

young (MODY)	younger patients developing symptoms similar to those with T2DM, i.e. asymptomatic hyperglycaemia with progression to more severe complications such as diabetic ketoacidosis
Latent autoimmune diabetes of adults (LADA)	The majority of patients with autoimmune-related diabetes present younger in life. There are however a small group of patients who develop such problems later in life. These patients are often misdiagnosed as having T2DM
Other types	Any pathological process which damages the insulin-producing cells of the pancreas may cause diabetes to develop. Examples include chronic pancreatitis and haemochromatosis. Drugs may also cause raised glucose levels. A common example is glucocorticoids which commonly result in raised blood glucose levels

Symptoms and signs

The presentation of diabetes mellitus depends very much on the type:

Type 1 DM	Type 2 DM
Weight loss Polydipsia Polyuria May present with diabetic ketoacidosis • abdominal pain • vomiting • reduced consciousness level	Often picked up incidentally on routine blood tests Polydipsia Polyuria

Remember that the polyuria and polydipsia are due to water being 'dragged' out of the body due to the osmotic effects of excess blood glucose being excreted in the urine (glycosuria).

Investigations

There are 4 main ways to check blood glucose:

- a finger-prick bedside glucose monitor
- a one-off blood glucose. This may either be fasting or non-fasting
- a HbA1c. This measures the amount of glycosylated haemoglobin and represents the average blood glucose over the past 2-3 months
- a glucose tolerance test. In this test, a fasting blood glucose is taken after which a 75g glucose load is taken. After 2 hours a second blood glucose reading is then taken

The diagnostic criteria are determined by WHO.

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c for the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover

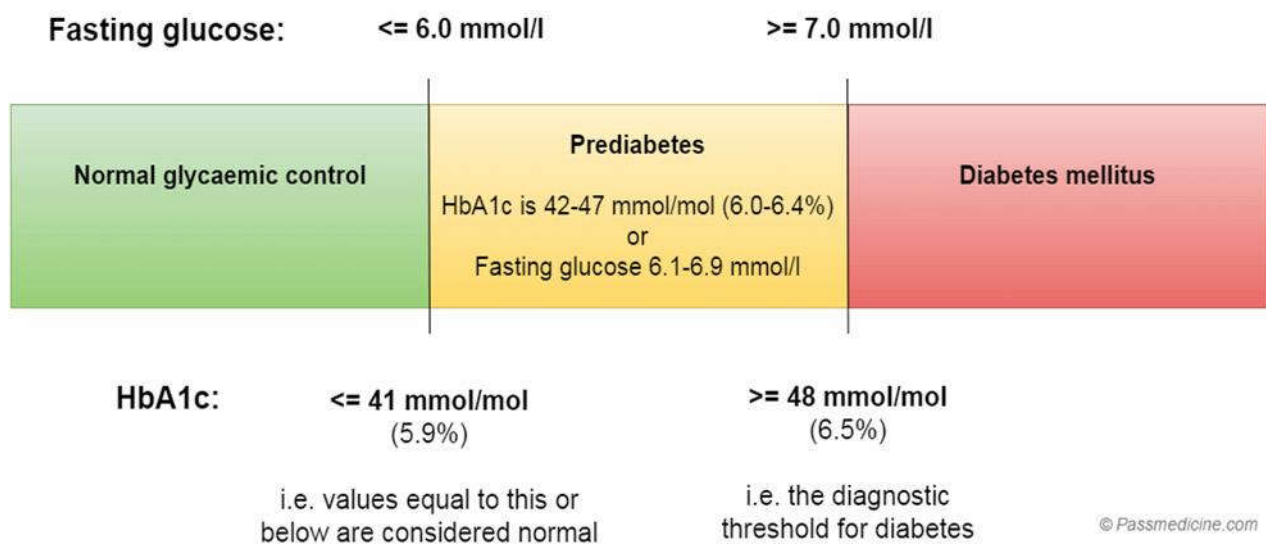


Diagram showing the spectrum of diabetes diagnosis

Management

The principle of managing diabetes mellitus are as follows:

- drug therapy to normalise blood glucose levels
- monitoring for and treating any complications related to diabetes
- modifying any other risk factors for other conditions such as cardiovascular disease

Type 1 diabetes

- patients always require insulin to control the blood sugar levels. This is because there is an absolute deficiency of insulin with no pancreatic tissue left to stimulate with drugs
- different types of insulin are available according to their duration of action

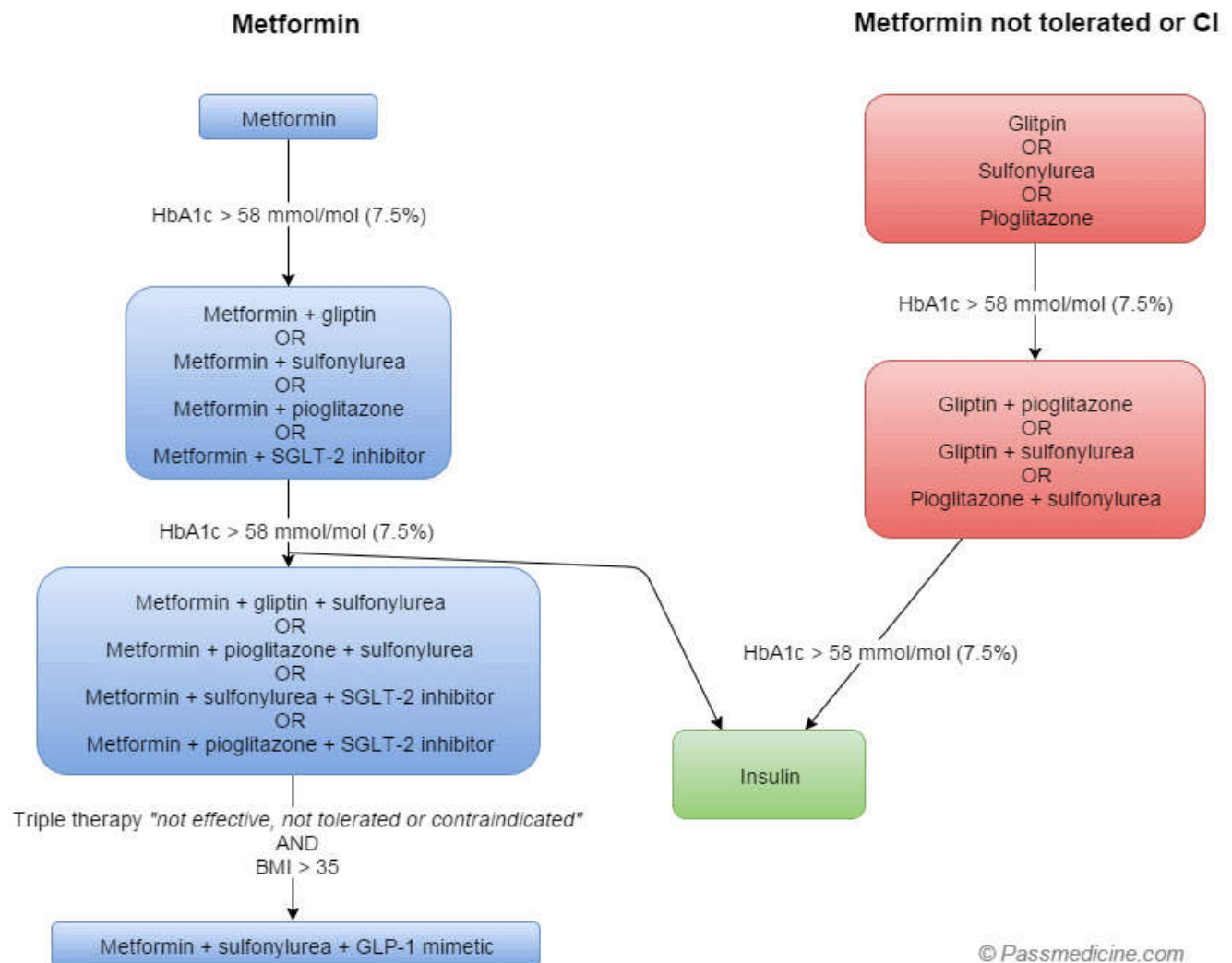
Type 2 diabetes

- the majority of patients with type 2 diabetes are controlled using oral medication
- the first-line drug for the vast majority of patients is metformin
- second-line drugs include sulfonylureas, gliptins and pioglitazone. Please see the table below for further information
- if oral medication is not controlling the blood glucose to a sufficient degree then insulin is used

The table below shows some of the main drugs used in the management of diabetes mellitus:

Drug class	Mechanism of action	Route	Main side-effects	Notes
Insulin	Direct replacement for endogenous insulin	Subcutaneous	Hypoglycaemia Weight gain Lipodystrophy	Used in all patients with T1DM and some patients with poorly controlled T2DM Can be classified according to source (analogue, human sequence and porcine) and duration of action (short, immediate, long-acting)
Metformin	Increases insulin sensitivity Decreases hepatic gluconeogenesis	Oral	Gastrointestinal upset Lactic acidosis*	First-line medication in the management of T2DM Cannot be used in patients with an eGFR of < 30 ml/min
Sulfonylureas	Stimulate pancreatic beta cells to secrete insulin	Oral	Hypoglycaemia Weight gain Hyponatraemia	Examples include gliclazide and glimepiride
Thiazolidinediones	Activate PPAR-gamma receptor in adipocytes to promote adipogenesis and fatty acid uptake	Oral	Weight gain Fluid retention	Only currently available thiazolidinedione is pioglitazone
DPP-4 inhibitors (-gliptins)	Increases incretin levels which inhibit glucagon secretion	Oral	Generally well tolerated but increased risk of pancreatitis	
SGLT-2 inhibitors (-gliflozins)	Inhibits reabsorption of glucose in the kidney	Oral	Urinary tract infection	Typically result in weight loss
GLP-1 agonists (-tides)	Incretin mimetic which inhibits glucagon secretion	Subcutaneous	Nausea and vomiting Pancreatitis	Typically result in weight loss

NICE provide guidelines on how drug therapy should be used in T2DM:



***common in exams, much less common in clinical practice**

Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2015. Key points are listed below:

- HbA1c targets have changed. They are now dependent on what antidiabetic drugs a patient is receiving and other factors such as frailty
- there is more flexibility in the second stage of treating patients (i.e. after metformin has been started) - you now have a choice of 4 oral antidiabetic agents.

It's worthwhile thinking of the average patient who is taking metformin for T2DM, you can titrate up metformin and encourage lifestyle changes to aim for a HbA1c of 48 mmol/mol (6.5%), but should only add a second drug if the HbA1c rises to 58 mmol/mol (7.5%)

Dietary advice:

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c targets

This is area which has changed in 2015

- individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 3-6 months until stable, then 6 monthly
- NICE encourage us to consider relaxing targets on '*a case-by-case basis, with particular consideration for people who are older or frail, for adults with type 2 diabetes*'
- in 2015 the guidelines changed so HbA1c targets are now dependent on treatment:

Lifestyle or single drug treatment

Management of T2DM	HbA1c target
Lifestyle	48 mmol/mol (6.5%)
Lifestyle + metformin	48 mmol/mol (6.5%)
Includes any drug which may cause hypoglycaemia (e.g. lifestyle + sulfonylurea)	53 mmol/mol (7.0%)

Practical examples

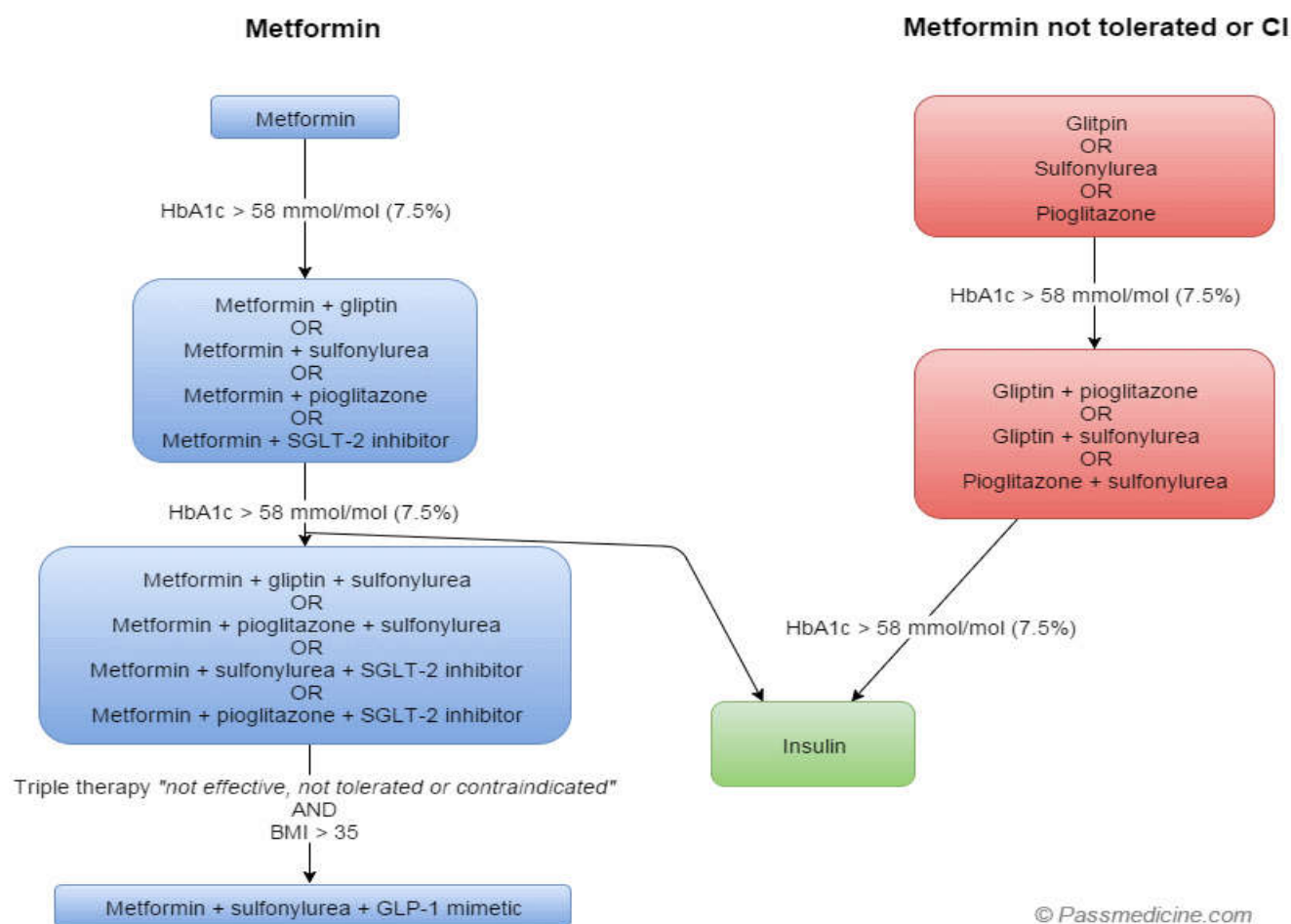
- a patient is newly diagnosed with HbA1c and wants to try lifestyle treatment first. You agree a target of 48 mmol/mol (6.5%)
- you review a patient 6 months after starting metformin. His HbA1c is 51 mmol/mol (6.8%). You increase his metformin from 500mg bd to 500mg tds and reinforce lifestyle factors

Patient already on treatment

Management of T2DM	HbA1c target
Already on one drug, but HbA1c has risen to 58 mmol/mol (7.5%)	53 mmol/mol (7.0%)

Drug treatment

The 2015 NICE guidelines introduced some changes into the management of type 2 diabetes. **There are essentially two pathways, one for patients who can tolerate metformin, and one for those who can't:**



Tolerates metformin:

- metformin is still first-line and should be offered if the HbA1c rises to 48 mmol/mol (6.5%)* on lifestyle interventions
- if the HbA1c has risen to 58 mmol/mol (7.5%) then a second drug should be added from the following list:
 - sulfonylurea
 - gliptin
 - pioglitazone
 - SGLT-2 inhibitor.

◆if despite this the HbA1c rises to, or remains above 58 mmol/mol (7.5%) then triple therapy with **one of the following combinations should be offered:**

- → metformin + gliptin + sulfonylurea.
- → metformin + pioglitazone + sulfonylurea.
- → metformin + sulfonylurea + SGLT-2 inhibitor.
- → metformin + pioglitazone + SGLT-2 inhibitor.
- → OR insulin therapy should be considered.

Criteria for glucagon-like peptide1 (GLP1) mimetic (e.g. exenatide):

- if triple therapy is not effective, not tolerated or contraindicated then NICE advise that we consider combination therapy with metformin, **a sulfonylurea and a glucagonlike peptide1 (GLP1) mimetic if:**
- → BMI ≥ 35 kg/m² and specific psychological or other medical problems associated with obesity or
- → BMI < 35 kg/m² and for whom insulin therapy would have significant occupational implications or

weight loss would benefit other significant obesityrelated comorbidities

- only continue if there is a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months

Practical examples

- you review an established type 2 diabetic on maximum dose metformin. Her HbA1c is 55 mmol/mol (7.2%). You do not add another drug as she has not reached the threshold of 58 mmol/mol (7.5%)
- a type 2 diabetic is found to have a HbA1c of 62 mmol/mol (7.8%) at annual review. They are currently on maximum dose metformin. You elect to add a sulfonylurea

Cannot tolerate metformin or contraindicated

- if the HbA1c rises to 48 mmol/mol (6.5%)* on lifestyle interventions, **consider one of the following:**
- → sulfonylurea
- → gliptin
- → pioglitazone
- if the HbA1c has risen to 58 mmol/mol (7.5%) then a one of the following combinations should be used:
- → gliptin + pioglitazone
- → gliptin + sulfonylurea
- → pioglitazone + sulfonylurea

- if despite this the HbA1c rises to, or remains above 58 mmol/mol (7.5%) then consider insulin therapy.

Starting insulin

- metformin should be continued. In terms of other drugs NICE advice: *'Review the continued need for other blood glucose lowering therapies'*
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

Risk factor modification

Blood pressure

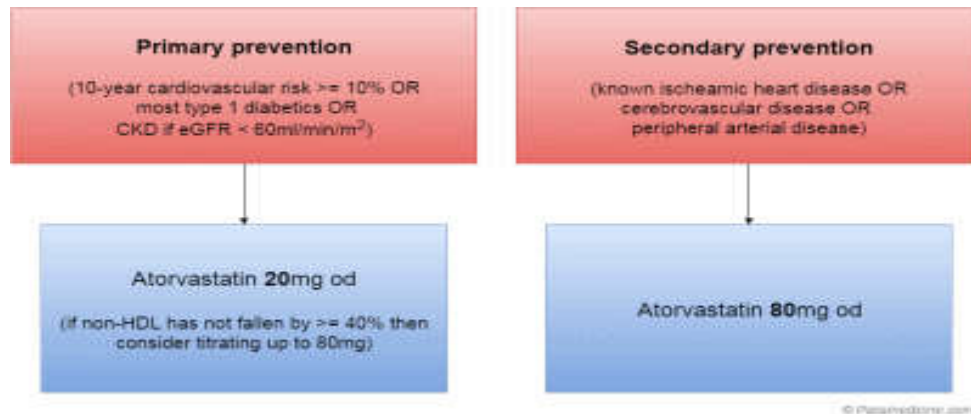
- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

Antiplatelets

- should not be offered unless a patient has existing cardiovascular disease

Lipids

- following the 2014 NICE lipid modification guidelines only patients with a 10-year cardiovascular risk > 10% (using QRISK2) should be offered a statin. The first-line statin of choice is atorvastatin 20mg on



Graphic showing choice of statin.

*this is a bit confusing because isn't the diagnostic criteria for T2DM HbA1c $\geq 48\text{ mmol/mol}$ (6.5%)? So shouldn't all patients be offered metformin at diagnosis? Our interpretation of this is that some patients upon diagnosis will elect to try lifestyle measures, which may reduce their HbA1c below this level. If it then rises to the diagnostic threshold again metformin should be offered

External Links

[NICE](#)

2015 Type 2 diabetes guidelines

[SIGN](#)

2010 Management of diabetes

[NICE](#)

2014 Lipid modification guidelines

Diabetes mellitus: Ramadan

◆We know that type 2 diabetes mellitus is more common in people of Asian ethnicity and a significant proportion of those patients in the UK will be Muslim. The BMJ published an excellent and comprehensive review of this issue in 2010¹.

◆It is important that we can give appropriate advice to Muslim patients to allow them safely observe their fast. This is particularly important from 2014 as Ramadan is due to fall in the long days of the summer months for several years henceforth.

◆Clearly it is a personal decision whether a patient decides to fast. It may however be worthwhile exploring the fact that people with chronic conditions are exempt from fasting or may be able to delay fasting to the shorter days of the winter months. It is however known that many Muslim patients with diabetes do not class themselves as having a chronic/serious condition which should exempt them from fasting. Around 79% of Muslim patients with type 2 diabetes mellitus fast Ramadan². There is an excellent patient information leaflet from Diabetes UK and the Muslim Council of Britain which explores these options in more detail.

◆If a patient with type 2 diabetes mellitus does decide to fast:

- they should try and eat a meal containing long-acting carbohydrates prior to sunrise (Suhor)
- patients should be given a blood glucose monitor to allow them to check their glucose levels, particularly if they feel unwell
- for patients taking metformin the expert consensus is that the dose should be split one-third before sunrise (Suhor) and two-thirds after sunset (Iftar)
- expert consensus also recommends switching once-daily sulfonylureas to after sunset. For patients taking twice-daily preparations such as gliclazide it is recommended that a larger proportion of the dose is taken after sunset
- no adjustment is needed for patients taking pioglitazone

1. Management of people with diabetes wanting to fast during Ramadan BMJ 2010;340:c3053

2. Salti I et al. Results of the Epidemiology of Diabetes and Ramadan (EPIDIAR) study. Diabetes Care 2004;27:2306-11.

External Links

[Diabetes Care](#)

Recommendations for Management of Diabetes During Ramadan

[Diabetes UK and Muslim Council](#)

Patient information leaflet on the management of diabetes during Ramadan

Diabetes: pathophysiology

Type 1 DM

- autoimmune disease
 - antibodies against beta cells of pancreas
 - HLA DR4 > HLA DR3
 - various antibodies such as islet-associated antigen (IAA) antibody and glutamic acid decarboxylase (GAD) antibody are detected in patients who later go on to develop type 1 DM - their prognostic significance is not yet clear
-

Diabetic ketoacidosis

Diabetic ketoacidosis may be a complication existing type 1 diabetes mellitus or be the first presentation, accounting for around 6% of cases. Whilst DKA remains a serious condition mortality rates have decreased from 8% to under 1% in the past 20 years.

The most common precipitating factors of DKA are infection, missed insulin doses and myocardial infarction

Features:

- abdominal pain
- polyuria, polydipsia, dehydration
- Kussmaul respiration (deep hyperventilation)
- Acetone-smelling breath ('pear drops' smell)

Diagnostic criteria

American Diabetes Association (2009)	Joint British Diabetes Societies (2013)
Key points - glucose > 13.8 mmol/l - pH < 7.30 - serum bicarbonate <18 mmol/l - anion gap > 10 - ketonaemia	Key points - glucose > 11 mmol/l or known diabetes mellitus - pH < 7.3 - bicarbonate < 15 mmol/l - ketones > 3 mmol/l or urine ketones ++ on dipstick

Management

- fluid replacement: most patients with DKA are deplete around 5-8 litres. Isotonic saline is used initially. Please see an example fluid regime below.
- insulin: an intravenous infusion should be started at 0.1 unit/kg/hour. Once blood glucose is < 15 mmol/l an infusion of 5% dextrose should be started
- correction of hypokalaemia

JBDS example of fluid replacement regime for patient with a sSystolic BP on admission 90mmHg and over

Fluid	Volume
0.9% sodium chloride 1L	1000ml over 1st hour
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 6 hours

Please note that slower infusion may be indicated in young adults (aged 18-25 years) as they are at greater risk of cerebral oedema.

JBDS potassium guidelines

Potassium level in first 24 hours (mmol/L)	Potassium replacement in mmol/L of infusion solution
Over 5.5	Nil
3.5-5.5	40
Below 3.5	Senior review as additional potassium needs to be given

Complications of DKA and its treatment:

- gastric stasis
- thromboembolism
- arrhythmias secondary to hyperkalaemia/iatrogenic hypokalaemia
- iatrogenic due to incorrect fluid therapy: cerebral oedema, hypokalaemia, hypoglycaemia
- acute respiratory distress syndrome
- acute kidney injury

External Links

[Diabetes Care](#)

Recommendations for Management of Diabetes During Ramadan

[Diabetes UK and Muslim Council](#)

Patient information leaflet on the management of diabetes during Ramadan

[Joint British Inpatient Diabetes Societies Inpatient Care Group](#)

The Management of Diabetic ketoacidosis in adults

Diabetic neuropathy

NICE updated it's guidance on the management of neuropathic pain in 2013. **Diabetic neuropathy is now managed in the same way as other forms of neuropathic pain:**

- first-line treatment: amitriptyline, duloxetine, gabapentin or pregabalin
- if the first-line drug treatment does not work try one of the other 3 drugs
- tramadol may be used as '*rescue therapy*' for exacerbations of neuropathic pain
- topical capsaicin may be used for localised neuropathic pain (e.g. post-herpetic neuralgia)
- pain management clinics may be useful in patients with resistant problems

Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

External Links

[NICE](#)

2013 Neuropathic pain guidelines

[NICE](#)

2015 Type 2 diabetes guidelines

Diabetic retinopathy

◆Diabetic retinopathy is the most common cause of blindness in adults aged 35-65 years-old. Hyperglycaemia is thought to cause increased retinal blood flow and abnormal metabolism in the retinal vessel walls. This precipitates damage to endothelial cells and pericytes

◆Endothelial dysfunction leads to increased vascular permeability which causes the characteristic exudates seen on fundoscopy. Pericyte dysfunction predisposes to the formation of microaneurysms. Neovascularization is thought to be caused by the production of growth factors in response to retinal ischaemia.

In exams you are most likely to be asked about the characteristic features of the various stages/types of diabetic retinopathy. Recently a new classification system has been proposed, dividing patients into those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative retinopathy (PDR):

Traditional classification	New classification
<u>Background retinopathy</u> - microaneurysms (dots) - blot haemorrhages (≤ 3) - hard exudates	<u>Mild NPDR</u> 1 or more microaneurysm
<u>Pre-proliferative retinopathy</u> - cotton wool spots (soft exudates; ischaemic nerve fibres) > 3 blot haemorrhages - venous beading/looping - deep/dark cluster haemorrhages - more common in Type I DM, treat with laser photocoagulation	<u>Moderate NPDR</u> - microaneurysms - blot haemorrhages - hard exudates - cotton wool spots, venous beading/looping and intraretinal microvascular abnormalities (IRMA) less severe than in severe NPDR
	<u>Severe NPDR</u> - blot haemorrhages and microaneurysms in 4 quadrants - venous beading in at least 2 quadrants - IRMA in at least 1 quadrant

Proliferative retinopathy

- retinal neovascularisation - may lead to vitreous haemorrhage
- fibrous tissue forming anterior to retinal disc
- more common in Type I DM, 50% blind in 5 years

Maculopathy

- based on location rather than severity, anything is potentially serious
- hard exudates and other 'background' changes on macula
- check visual acuity
- more common in Type II DM

External Links

[Birmingham University](#)

Diabetic retinopathy tutorial with fundoscopy images

Disorders of sex development

The table below lists the most common disorders of sex development:

Name	Karyotype	Notes
Androgen insensitivity syndrome	46 XY	X-linked recessive condition. Defect in androgen receptor results in end-organ resistance to testosterone causing genotypically male children (46XY) to have a female phenotype. Rudimentary vagina and testes present but no uterus. Testosterone, oestrogen and LH levels are elevated
5- α reductase deficiency	46 XY	Autosomal recessive condition. Results in the inability of males to convert testosterone to dihydrotestosterone (DHT). Individuals have ambiguous genitalia in the newborn period. Hypospadias is common. Virilization at puberty.

Male pseudohermaphroditism	46 XY	Individual has testes but external genitalia are female or ambiguous. may be secondary to androgen insensitivity syndrome
Female pseudohermaphroditism	46 XX	Individual has ovaries but external genitalia are male (virilized) or ambiguous. May be secondary to congenital adrenal hyperplasia
True hermaphroditism	46 XX or 47 XXY	Very rare, both ovarian and testicular tissue are present

DVLA: diabetes mellitus

Until recently people with diabetes who used insulin could not hold a HGV licence. The DVLA changed the rules in October 2011. **The following standards need to be met (and also apply to patients using other hypoglycaemic inducing drugs such as sulfonylureas):**

- there has not been any severe hypoglycaemic event in the previous 12 months
- the driver has full hypoglycaemic awareness
- the driver must show adequate control of the condition by regular blood glucose monitoring*, at least twice daily and at times relevant to driving
- the driver must demonstrate an understanding of the risks of hypoglycaemia
- there are no other debarring complications of diabetes

From a practical point of view patients on insulin who want to apply for a Group 2 (HGV) licence need to complete a VDIAB11 form.

Other specific points for group 1 drivers:

- if on insulin then patient can drive a car as long as they have hypoglycaemic awareness, not more than one episode of hypoglycaemia requiring the assistance of another person within the preceding 12 months and no relevant visual impairment. Drivers are normally contacted by DVLA
- if on tablets or exenatide no need to notify DVLA. If tablets may induce hypoglycaemia (e.g. sulfonylureas) then there must not have been more than one episode of hypoglycaemia requiring the assistance of another person within the preceding 12 months
- if diet controlled alone then no requirement to inform DVLA

*to demonstrate adequate control, the Secretary of State's Honorary Medical Advisory Panel on Diabetes Mellitus has recommended that applicants will need to have used blood glucose meters with a memory function to measure and record blood glucose levels for at least 3 months prior to submitting their application

External Links

[DVLA](#)

Diabetes mellitus guidelines

[Gov.uk](#)

Diabetes and driving.

Dynamic pituitary function tests

A dynamic pituitary function test is used to assess patients with suspected primary pituitary dysfunction

Insulin, TRH and LHRH are given to the patient following which the serum glucose, cortisol, growth hormone, TSH, LH and FSH levels are recorded at regular intervals. Prolactin levels are also sometimes measured*

A normal dynamic pituitary function test has the following characteristics:

- GH level rises $> 20\text{mu/l}$
- cortisol level rises $> 550\text{ mmol/l}$
- TSH level rises by $> 2\text{ mu/l}$ from baseline level
- LH and FSH should double

*dopamine antagonist tests using metoclopramide may also be used in the investigation of hyperprolactinaemia. A normal response is at least a twofold rise in prolactin. A blunted prolactin response suggests a prolactinoma

Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) $> 7.5\text{ mmol/l}$ and LDL-C $> 4.9\text{ mmol/l}$ or children TC $> 6.7\text{ mmol/l}$ and LDL-C $> 4.0\text{ mmol/l}$, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

Management:

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening. This includes children who should be screened by the age of 10 years if there is one affected parent
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

External Links

[NICE](#)

2008 Familial hypercholesterolaemia guidelines

[Public Library of Science \(PLOS\)](#)

Cascade Screening for Familial Hypercholesterolemia (FH)

[Heart UK](#)

Simon Broome criteria

[Familial Hypercholesterolaemia Foundation](#)

High cholesterol during pregnancy

Gitelman's syndrome

Gitelman's syndrome is due to a defect in the thiazide-sensitive Na⁺ Cl⁻ transporter in the distal convoluted tubule.

Features

- hypokalaemia
- hypomagnesaemia
- hypocalciuria
- metabolic alkalosis
- normotension.

Glycosylated hemoglobin

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on:

- red blood cell lifespan
- average blood glucose concentration

A number of conditions can interfere with accurate HbA1c interpretation:

Lower-than-expected levels of HbA1c (due to reduced red blood cell lifespan)	Higher-than-expected levels of HbA1c (due to increased red blood cell lifespan)
Sickle-cell anemia GP6D deficiency Hereditary spherocytosis	Vitamin B12/folic acid deficiency Iron-deficiency anemia Splenectomy

◆HbA1c is generally thought to reflect the blood glucose over the previous '3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks. NICE recommend '*HbA1c should be checked every 3-6 months until stable, then 6 monthly*'.

◆The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HbA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose = $(2 * \text{HbA1c}) - 4.5$

External Links

[DocStoc](#)

HbA1c conversion chart

Graves' disease: features

Graves' disease is the most common cause of thyrotoxicosis. It is typically seen in women aged 30-50 years.

Features

- typical features of thyrotoxicosis
- specific signs limited to Grave's (see below)

Features seen in Graves' but not in other causes of thyrotoxicosis

- eye signs (30% of patients): exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

Autoantibodies

- TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (75%)

Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime.

Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Causes of gynaecomastia

- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below.

Drug causes of gynaecomastia

- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- gonadorelin analogues e.g. Goserelin, buserelin
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia

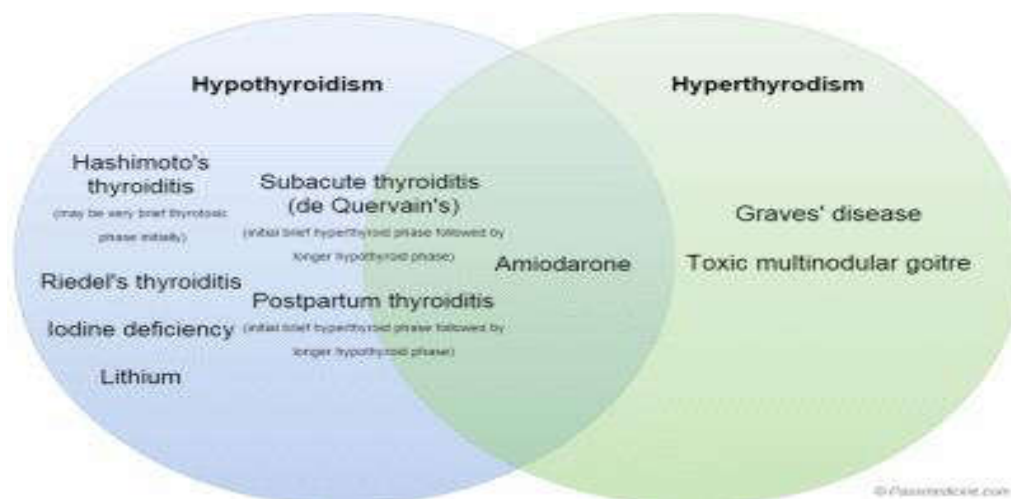
- tricyclics
 - isoniazid
 - calcium channel blockers
 - heroin
 - busulfan
 - methyldopa
-

Hashimoto's thyroiditis

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

Features:

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

Hypercalcemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

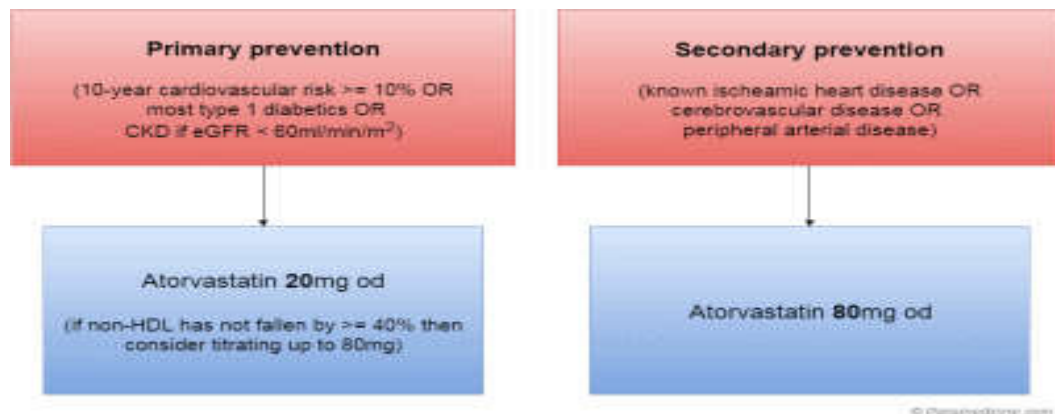
- sarcoidosis*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone**

*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

**usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Hyperlipidaemia: management

In 2014 NICE updated their guidelines on lipid modification. This proved highly controversial as it meant that we should be recommending statins to a significant proportion of the population over the age of 60 years. Anyway, the key points of the new guidelines are summarised below.



Graphic showing choice of statin.

Primary prevention - who and how to assess risk

A systematic strategy should be used to identify people aged over 40 years who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of **10%** or greater.

NICE recommend we use the **QRISK2** CVD risk assessment tool for patients aged ≤ 84 years. Patients ≥ 85 years are at high risk of CVD due to their age. QRISK2 should not be used in the following situations as there are more specific guidelines for these patient groups:

- type 1 diabetics
- patients with an estimated glomerular filtration rate (eGFR) less than 60 ml/min and/or albuminuria
- patients with a history of familial hyperlipidaemia.

NICE suggest QRISK2 may underestimate CVD risk in the following population groups:

- people treated for HIV
- people with serious mental health problems
- people taking medicines that can cause dyslipidaemia such as antipsychotics, corticosteroids or immunosuppressant drugs
- people with autoimmune disorders/systemic inflammatory disorders such as systemic lupus erythematosus

Measuring lipid levels

When measuring lipids both the total cholesterol and HDL should be checked to provide the most accurate risk of CVD. A full lipid profile should also be checked (i.e. including triglycerides) before starting a statin. The samples does not need to be fasting.

In the vast majority of patient the cholesterol measurements will be fed into the QRISK2 tool. If however the patient's cholesterol is very high we should consider familial hyperlipidaemia. NICE recommend the following that we should consider the possibility of familial hypercholesterolaemia and investigate further if the total cholesterol concentration is > 7.5 mmol/l and there is a family history of premature coronary heart disease. They also recommend referring people with a total cholesterol > 9.0 mmol/l or a non-HDL cholesterol (i.e. LDL) of > 7.5 mmol/l even in the absence of a first-degree family history of premature coronary heart disease.

Interpreting the QRISK2 result

Probably the headline changes in the 2014 guidelines was the new, lower cut-off of 10-year CVD risk cut-off of 10%.

NICE now recommend we offer a statin to people with a QRISK2 10-year risk of $\geq 10\%$

Lifestyle factors are of course important and NICE recommend that we give patients the option of having their CVD risk reassessed after a period of time before starting a statin.

Atorvastatin 20mg should be offered first-line.

Special situations

Type 1 diabetes mellitus

- NICE recommend that we 'consider statin treatment for the primary prevention of CVD in all adults with type 1 diabetes'
- atorvastatin 20 mg should be offered if type 1 diabetics who are:
 - older than 40 years, or
 - have had diabetes for more than 10 years or
 - have established nephropathy or
 - have other CVD risk factors

Chronic kidney disease (CKD)

- atorvastatin 20mg should be offered to patients with CKD
- increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved and the eGFR > 30 ml/min. If the eGFR is < 30 ml/min a renal specialist should be consulted before increasing the dose

Secondary prevention

All patients with CVD should be taking a statin in the absence of any contraindication.

Atorvastatin 80mg should be offered first-line.

Follow-up of people started on statins

NICE recommend we follow-up patients at 3 months

- repeat a full lipid profile
- if the non-HDL cholesterol has not fallen by at least 40% concordance and lifestyle changes should be discussed with the patient
- NICE recommend we consider increasing the dose of atorvastatin up to 80mg

Lifestyle modifications:

These are in many ways predictable but NICE make a number of specific points:

Cardio protective diet

- total fat intake should be $\leq 30\%$ of total energy intake
- saturated fats should be $\leq 7\%$ of total energy intake
- intake of dietary cholesterol should be < 300 mg/day
- saturated fats should be replaced by monounsaturated and polyunsaturated fats where possible
- replace saturated and monounsaturated fat intake with olive oil, rapeseed oil or spreads based on these oils
- choose wholegrain varieties of starchy food
- reduce their intake of sugar and food products containing refined sugars including fructose
- eat at least 5 portions of fruit and vegetables per day
- eat at least 2 portions of fish per week, including a portion of oily fish
- eat at least 4 to 5 portions of unsalted nuts, seeds and legumes per week

Physical activity

- each week aim for at least 150 minutes of moderate intensity aerobic activity or 75 minutes of vigorous intensity aerobic activity or a mix of moderate and vigorous aerobic activity
- do musclestrengthening activities on 2 or more days a week that work all major muscle groups (legs, hips, back, abdomen, chest, shoulders and arms) in line with national guidance for the general population

Weight management

- no specific advice is given, overweight patients should be managed in keeping with relevant NICE guidance

Alcohol intake

- again no specific advice, other than the general recommendation that males drink no more than 3-4 units/day and females no more than 2-3 units/day

Smoking cessation

- smokers should be encouraged to quit

External Links

[NICE](#)

2014 Lipid modification guidelines

[Clinical Knowledge Summaries](#)

Managing lipids in type 2 diabetes

Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia

- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia

- nephrotic syndrome
 - cholestasis
 - hypothyroidism
-

Hyperosmolar hyperglycaemic state

Hyperosmolar hyperglycaemic state (HHS) is confirmed by:

- Dehydration
- Osmolality $>320\text{mosmol/kg}$
- Hyperglycaemia $>30\text{ mmol/L}$ with pH >7.3 , bicarbonate $>15\text{mmol/L}$ and no significant ketonenaemia $<3\text{mmol/L}$

External Links

[Joint British Diabetes Societies](#)

The management of the hyperosmolar hyperglycaemic state (HHS)

Hypoglycaemia

Causes

- insulinoma - increased ratio of proinsulin to insulin
- self-administration of insulin/sulphonylureas
- liver failure
- Addison's disease
- alcohol

Other possible causes in children

- nesidioblastosis - beta cell hyperplasia

External Links

[Postgraduate Medical Journal](#)

Review of endocrine emergencies

Hypoparathyroidism

Primary hypoparathyroidism

- decrease PTH secretion
- e.g. secondary to thyroid surgery*
- low calcium, high phosphate
- treated with alfacalcidol

The main symptoms of hypoparathyroidism are secondary to hypocalcaemia:

- tetany: muscle twitching, cramping and spasm
- perioral paraesthesia
- Trousseau's sign: carpal spasm if the brachial artery occluded by inflating the blood pressure cuff and maintaining pressure above systolic
- Chvostek's sign: tapping over parotid causes facial muscles to twitch
- if chronic: depression, cataracts
- ECG: prolonged QT interval

Pseudohypoparathyroidism

- target cells being insensitive to PTH
- due to abnormality in a G protein
- associated with low IQ, short stature, shortened 4th and 5th metacarpals
- low calcium, high phosphate, high PTH
- diagnosis is made by measuring urinary cAMP and phosphate levels following an infusion of PTH. In hypoparathyroidism this will cause an increase in both cAMP and phosphate levels. In pseudohypoparathyroidism type I neither cAMP nor phosphate levels are increased whilst in pseudohypoparathyroidism type II only cAMP rises.

Pseudopseudohypoparathyroidism

- similar phenotype to pseudohypoparathyroidism but normal biochemistry
*this may seem an oxymoron, but most medical textbooks classify hypoparathyroidism which is secondary to surgery as being 'primary hypoparathyroidism'

Hypothyroidism: causes

Hypothyroidism affects around 1-2% of women in the UK and is around 5-10 times more common in females than males.

Primary hypothyroidism

Hashimoto's thyroiditis

- most common cause
- autoimmune disease, associated with IDDM, Addison's or pernicious anaemia
- may cause transient thyrotoxicosis in the acute phase
- 5-10 times more common in women

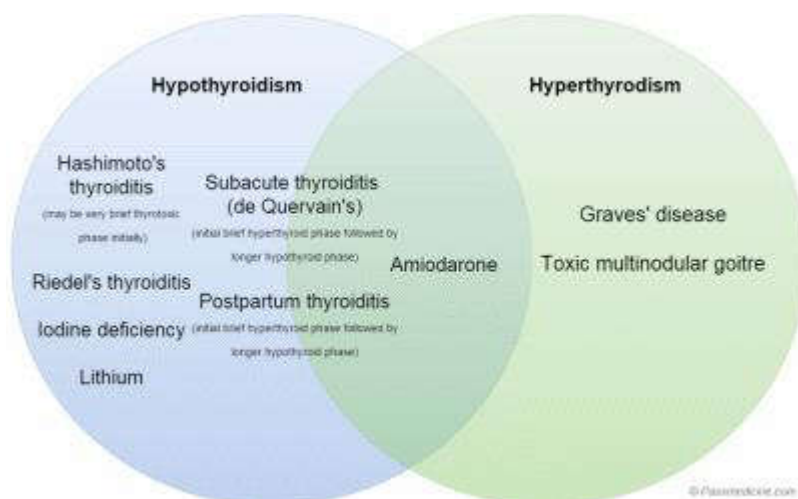
Subacute thyroiditis (de Quervain's)

Riedel thyroiditis

After thyroidectomy or radioiodine treatment

Drug therapy (e.g. lithium, amiodarone or anti-thyroid drugs such as carbimazole)

Dietary iodine deficiency



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

Secondary hypothyroidism (rare)

From pituitary failure

Other associated conditions

- Down's syndrome
- Turner's syndrome
- coeliac disease

Hypothyroidism: management

Key points:

- initial starting dose of levothyroxine should be lower in elderly patients and those with ischaemic heart disease. The BNF recommends that for patients with cardiac disease, severe hypothyroidism or patients over 50 years the initial starting dose should be 25mcg od with dose slowly titrated. Other patients should be started on a dose of 50-100mcg od
- following a change in thyroxine dose thyroid function tests should be checked after 8-12 weeks
- the therapeutic goal is 'normalisation' of the thyroid stimulating hormone (TSH) level. As the majority of unaffected people have a TSH value 0.5-2.5 mU/l it is now thought preferable to aim for a TSH in this range
- women with established hypothyroidism who become pregnant should have their dose increased 'by at least 25-50 micrograms levothyroxine'* due to the increased demands of pregnancy. The TSH should be monitored carefully, aiming for a low-normal value
- there is no evidence to support combination therapy with levothyroxine and liothyronine

Side-effects of thyroxine therapy

- hyperthyroidism: due to over treatment
- reduced bone mineral density
- worsening of angina
- atrial fibrillation

Interactions

- iron: absorption of levothyroxine reduced, give at least 2 hours apart

*source: NICE Clinical Knowledge Summaries

External Links

[Clinical Knowledge Summaries](#)

Management of hypothyroidism

Insulin stress test

Basics

- used in investigation of hypopituitarism
- IV insulin given, GH and cortisol levels measured
- with normal pituitary function GH and cortisol should rise

Contraindications

- epilepsy
 - ischaemic heart disease
 - adrenal insufficiency
-

Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

Basics

- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

Features

- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

Diagnosis

- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

Management

- surgery
 - diazoxide and somatostatin if patients are not candidates for surgery
-

Liddle's syndrome

Liddle's syndrome is a rare autosomal dominant condition that causes hypertension and hypokalaemic alkalosis. It is thought to be caused by disordered sodium channels in the distal tubules leading to increased reabsorption of sodium.

Treatment is with either amiloride or triamterene

Meglitinides

Meglitinides (e.g. repaglinide, nateglinide)

- insulin secretagogues
 - like sulfonylureas they bind to an ATP-dependent K^+ (K_{ATP}) channel on the cell membrane of pancreatic beta cells
 - often used for patients with an erratic lifestyle
 - adverse effects include weight gain and hypoglycaemia (less so than sulfonylureas)
-

Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. **For a diagnosis of metabolic syndrome at least 3 of the following should be identified:**

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for European men and > 80cm for European women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, **AND two of the following:**

- blood pressure: > 140/90 mmHg
- dyslipidaemia: triglycerides: > 1.695 mmol/L and/or high-density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- central obesity: waist:hip ratio > 0.90 (male), > 0.85 (female), and/or body mass index > 30 kg/m²
- microalbuminuria: urinary albumin excretion ratio > 20 mg/min or albumin:creatinine ratio > 30 mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

External Links

[SIGN](#)

Risk estimation and the prevention of cardiovascular disease

MODY

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY.

It is thought that around 1-2% of patients with diabetes mellitus have MODY, and around 90% are misclassified as having either type 1 or type 2 diabetes mellitus.

MODY 3

- 60% of cases
- due to a defect in the HNF-1 alpha gene

MODY 2

- 20% of cases
- due to a defect in the glucokinase gene

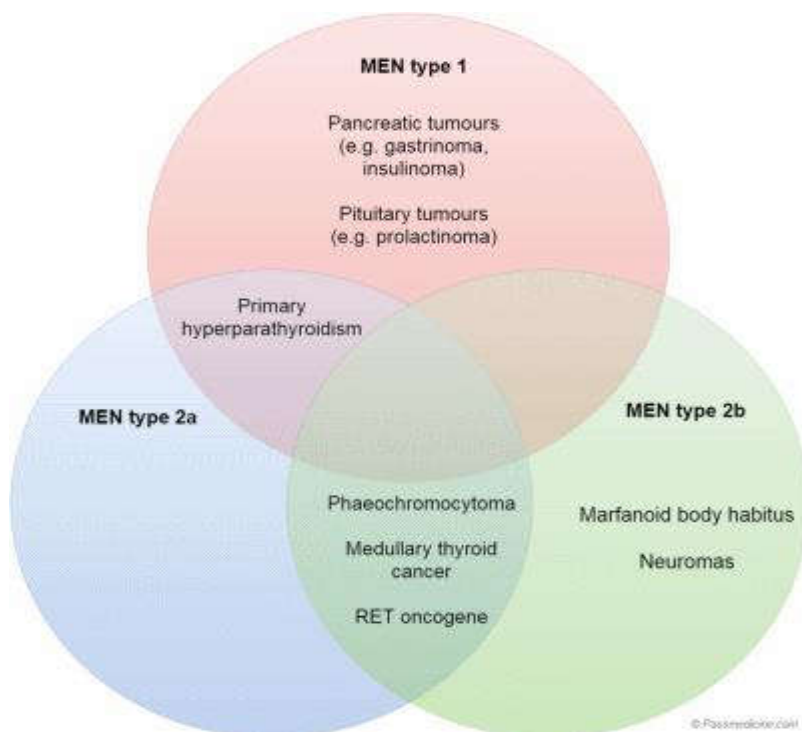
Features of MODY

- typically develops in patients < 25 years
- a family history of early onset diabetes is often present
- ketosis is not a feature at presentation
- patients with the most common form are very sensitive to sulfonylureas, insulin is not usually necessary

Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN). MEN is inherited as an autosomal dominant disorder.

MEN type I	MEN type IIa	MEN type IIb
3 P's P arathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia P ituitary (70%) P ancreas (50%): e.g. insulinoma, gastrinoma (leading to recurrent peptic ulceration) Also: adrenal and thyroid	Medullary thyroid cancer (70%) 2 P's P arathyroid (60%) P haeochromocytoma	Medullary thyroid cancer 1 P P haeochromocytoma Marfanoid body habitus Neuromas
MEN1 gene Most common presentation = hypercalcaemia	RET oncogene	RET oncogene



Venn diagram showing the different types of MEN and their associated features

Neuroblastoma

◆Neuroblastoma is one of the top five causes of cancer in children, accounting for around 7-8% of childhood malignancies. The tumour arises from neural crest tissue of the adrenal medulla (the most common site) and sympathetic nervous system.

◆Median age of onset is around 20 months.

Features:

- abdominal mass
- pallor, weight loss
- bone pain, limp
- hepatomegaly
- paraplegia
- proptosis

Investigation

- raised urinary vanillylmandelic acid (VMA) and homovanillic acid (HVA) levels
- calcification may be seen on abdominal x-ray
- biopsy.

Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m^2 or more, or between 35 kg/m^2 and 40 kg/m^2 and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up.

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m² in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long.

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery.

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m²
- patients with a BMI > 40 kg/m² may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m²)

External Links

[NICE](#)

2014 Obesity guidelines

Obesity: therapeutic options

The management of obesity consists of a step-wise approach:

- conservative: diet, exercise
- medical
- surgical

Orlistat is a pancreatic lipase inhibitor used in the management of obesity. Adverse effects include faecal urgency/incontinence and flatulence. A lower dose version is now available without prescription ('Alli'). NICE have defined criteria for the use of orlistat. It should only be prescribed as part of an overall plan for managing obesity in adults who have:

- BMI of 28 kg/m² or more with associated risk factors, or
- BMI of 30 kg/m² or more
- continued weight loss e.g. 5% at 3 months
- orlistat is normally used for < 1 year

Sibutramine

- withdrawn January 2010 by the European Medicines Agency due to an increased risk of cardiovascular events
- centrally acting appetite suppressant (inhibits uptake of serotonin and noradrenaline at hypothalamic sites that regulate food intake)
- adverse effects include hypertension (monitor blood pressure and pulse during treatment), constipation, headache, dry mouth, insomnia and anorexia
- contraindicated in psychiatric illness, hypertension, IHD, stroke, arrhythmias.

Rimonabant, a specific CB1 cannabinoid receptor antagonist, was withdrawn in October 2008 after the European Medicines Agency warned of serious psychiatric problems including suicide

External Links

[NICE](#)

Obesity guidelines

Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include: bone pain, skull or long bone deformity, fracture, periarticular
Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure



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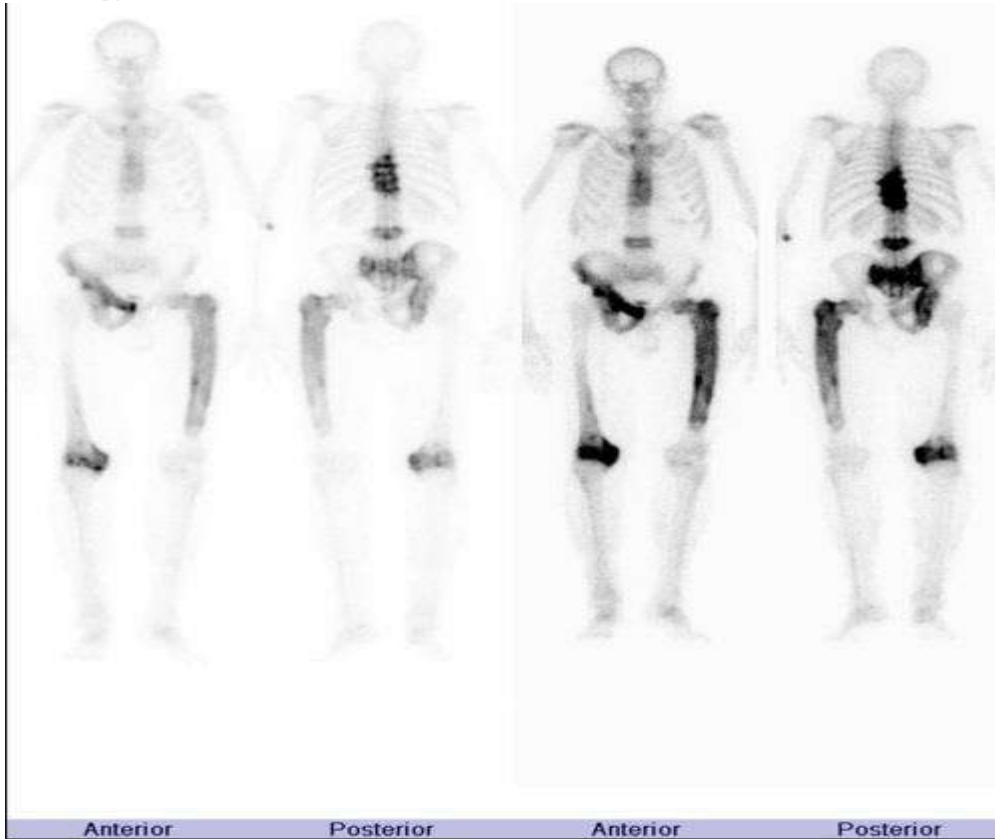
The radiograph demonstrates marked thickening of the calvarium. There are also ill-defined sclerotic and lucent areas throughout. These features are consistent with Paget's disease.



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Pelvic x-ray from an elderly man with Paget's disease. There is a smooth cortical expansion of the left hemipelvic bones with diffuse increased bone density and coarsening of trabeculae.



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Isotope bone scan from a patient with Paget's disease showing a typical distribution in the spine, asymmetrical pelvic disease and proximal long bones.

*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Pender's syndrome

- ◆Pendred is an autosomal recessive genetic disorder that is characterised by bilateral sensorineural deafness, with mild hypothyroidism and a goitre. The patients tend to present with progressive hearing loss and delay in academic progression. Often head trauma tends to make the sensorineural deafness worse, leading to patients having to avoid contact sports.
- ◆In Pendred syndrome there is a defect in the organification of iodine, leading to dyshormonogenesis. However thyroid symptoms in pendred syndrome are often mild and patients are often clinically euthyroid, presenting only with a goitre. Thyroid function tests are also often normal, requiring the perchlorate discharge test to aid diagnosis.
- ◆The syndrome can be diagnosed via genetic testing (Pendred syndrome (PDS) gene, chromosome 7), audiometry and MRI imaging to look for characteristic one and a half turns in the cochlea, compared to the normal two and a half turns.
- ◆Treatment is with thyroid hormone replacement and cochlear implants.

Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

Basics:

- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

Features are typically episodic

- hypertension (around 90% of cases, may be sustained)
- headaches
- palpitations
- sweating
- anxiety.

Tests

- 24 hr urinary collection of metanephrines (sensitivity 97%*)
- this has replaced a 24 hr urinary collection of catecholamines (sensitivity 86%)

Surgery is the definitive management. **The patient must first however be stabilized with medical management:**

- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

*BMJ 2012; 344 doi: <http://dx.doi.org/10.1136/bmj.e1042> (Published 20 February 2012)

External Links

[Postgraduate Medical Journal](#)

Review of endocrine emergencies

Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

Features:

- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsutism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

Investigations:

- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful in diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies. NICE updated the guidance in 2015

Risk factors for gestational diabetes:

- BMI of $> 30 \text{ kg/m}^2$
- previous macrosomic baby weighing 4.5 kg or above
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- women who've previously had gestational diabetes: oral glucose tolerance test (OGTT) should be performed as soon as possible after booking and at 24-28 weeks if the first test is normal. NICE also recommend that early self-monitoring of blood glucose is an alternative to the OGTTs
- women with any of the other risk factors should be offered an OGTT at 24-28 weeks.

Diagnostic thresholds for gestational diabetes:

- these have recently been updated by NICE, gestational diabetes is diagnosed if either:
- fasting glucose is ≥ 5.6 mmol/l
- 2-hour glucose is ≥ 7.8 mmol/l

Management of gestational diabetes

- newly diagnosed women should be seen in a joint diabetes and antenatal clinic within a week
- women should be taught about selfmonitoring of blood glucose
- advice about diet (including eating foods with a low glycaemic index) and exercise should be given
- if the fasting plasma glucose level is < 7 mmol/l a trial of diet and exercise should be offered
- if glucose targets are not met within 1-2 weeks of altering diet/exercise metformin should be started
- if glucose targets are still not met insulin should be added to diet/exercise/metformin
- if at the time of diagnosis the fasting glucose level is ≥ 7 mmol/l insulin should be started
- if the plasma glucose level is between 6-6.9 mmol/l, and there is evidence of complications such as macrosomia or hydramnios, insulin should be offered
- glibenclamide should only be offered for women who cannot tolerate metformin or those who fail to meet the glucose targets with metformin but decline insulin treatment

Management of pre-existing diabetes

- weight loss for women with BMI of > 27 kg/m²
- stop oral hypoglycaemic agents, apart from metformin, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy.

♦Targets for self-monitoring of pregnant women (pre-existing and gestational diabetes):

Time	Target
Fasting	5.3 mmol/l
1 hour after meals	7.8 mmol/l, or:
2 hour after meals	6.4 mmol/l

External Links

[NICE](#)

2015 Management of diabetes in pregnancy

[Postgraduate Medical Journal](#)

DKA in pregnancy

Pregnancy: thyroid problems

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level.

Thyrotoxicosis

Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

Management

- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism
- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated.

Hypothyroidism

Key points

- thyroxine is safe during pregnancy
- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine

External Links

[The Endocrine Society](#)

Management of Thyroid Dysfunction during Pregnancy and Postpartum

Primary hyperparathyroidism

In exams, primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism

- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'

- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension.

Associations

- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations

- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

Treatment

- total parathyroidectomy



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Bilateral hand radiographs in a middle-aged woman demonstrating generalised osteopenia, erosion of the terminal phalangeal tufts (acro-osteolysis) and subperiosteal resorption of bone particularly the radial aspects of the 2nd and 3rd middle phalanges. These changes are consistent with a diagnosis of hyperparathyroidism.

Remnant hyperlipidemia

Overview

- rare cause of mixed hyperlipidaemia (raised cholesterol and triglyceride levels)
- also known as Fredrickson type III hyperlipidaemia, broad-beta disease and dysbetalipoproteinaemia
- associated with apo-e2 homozygosity
- high incidence of ischaemic heart disease and peripheral vascular disease
- thought to be caused by impaired removal of intermediate density lipoprotein from the circulation by the liver.

Features

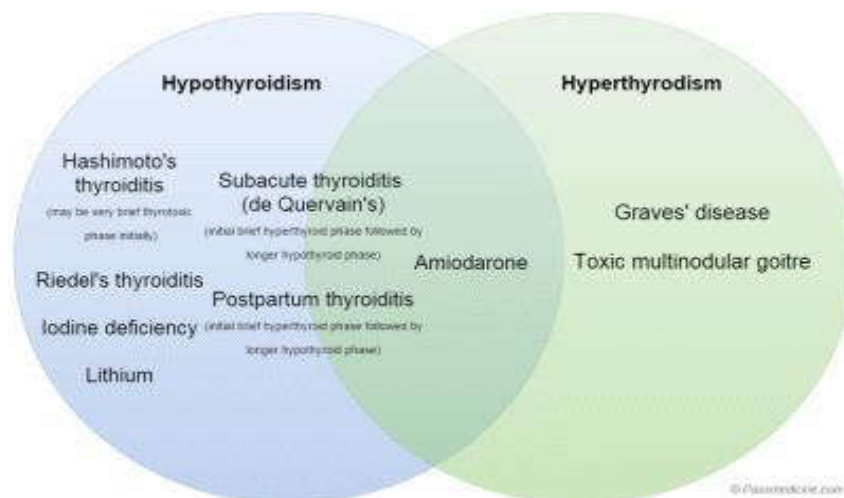
- yellow palmar creases
- palmer xanthomas
- tuberous xanthomas

Management

- fibrates are first line treatment

Riedel's thyroiditis

Riedel's thyroiditis is a rare cause of hypothyroidism characterised by dense fibrous tissue replacing the normal thyroid parenchyma. On examination a hard, fixed, painless goitre is noted. It is usually seen in middle-aged women. It is associated with retroperitoneal fibrosis.



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

SGLT2 inhibitors

SGLT2 inhibitors reversibly inhibit sodium-glucose co-transporter 2 (SGLT2) in the renal proximal convoluted tubule to reduce glucose reabsorption and increase urinary glucose excretion.

Examples include canagliflozin, dapagliflozin and empagliflozin

Important adverse effects include:

- genital infection (secondary to glycosuria)
 - diabetic ketoacidosis
-

Sick euthyroid syndrome

In sick euthyroid syndrome (now referred to as non-thyroidal illness) it is often said that everything (TSH, thyroxine and T3) is low. In the majority of cases however the TSH level is within the normal range (inappropriately normal given the low thyroxine and T3).

Changes are reversible upon recovery from the systemic illness.

Skin disorders associated with thyroid disease

Skin manifestations of hypothyroidism

- dry (anhydrosis), cold, yellowish skin
- non-pitting oedema (e.g. hands, face)
- dry, coarse scalp hair, loss of lateral aspect of eyebrows
- eczema
- xanthomata

Skin manifestations of hyperthyroidism

- pretibial myxoedema: erythematous, oedematous lesions above the lateral malleoli
- thyroid acropachy: clubbing
- scalp hair thinning
- increased sweating

Pruritus can occur in both hyper- and hypothyroidism.

External Links

DermIS.net

Pictures of pretibial myxoedema

Subacute (De Quervain's) thyroiditis

Subacute thyroiditis (also known as De Quervain's thyroiditis and subacute granulomatous thyroiditis) is thought to occur following viral infection and typically presents with hyperthyroidism.

There are typically 4 phases:

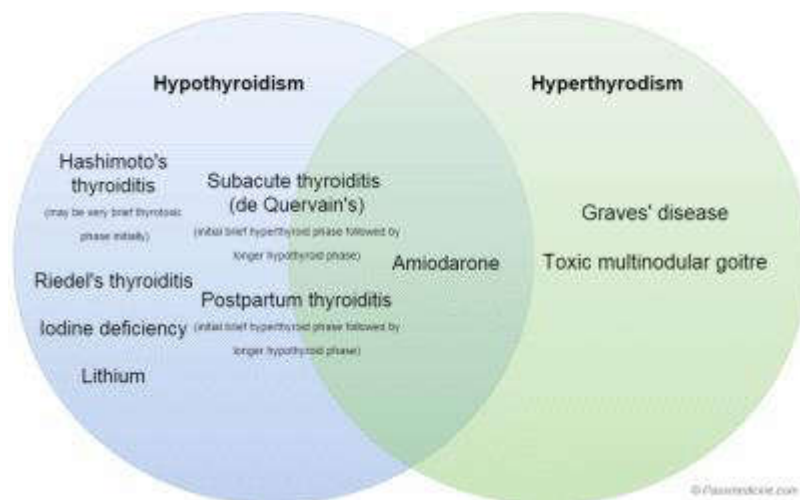
- phase 1 (lasts 3-6 weeks): hyperthyroidism, painful goitre, raised ESR
- phase 2 (1-3 weeks): euthyroid
- phase 3 (weeks - months): hypothyroidism
- phase 4: thyroid structure and function goes back to normal

Investigations

- globally reduced uptake on iodine-131 scan

Management

- usually self-limiting - most patients do not require treatment
- thyroid pain may respond to aspirin or other NSAIDs
- in more severe cases steroids are used, particularly if hypothyroidism develops.



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

Subclinical hyperthyroidism

Subclinical hyperthyroidism is an entity which is gaining increasing recognition. **It is defined as:**

- normal serum free thyroxine and triiodothyronine levels
- with a thyroid stimulating hormone (TSH) below normal range (usually < 0.1 mu/l)

Causes

- multinodular goitre, particularly in elderly females
- excessive thyroxine may give a similar biochemical picture

The importance in recognising subclinical hyperthyroidism lies in the potential effect on the cardiovascular system (atrial fibrillation) and bone metabolism (osteoporosis). It may also impact on quality of life and increase the likelihood of dementia

Management

- TSH levels often revert to normal - therefore levels must be persistently low to warrant intervention.
- a reasonable treatment option is a therapeutic trial of low-dose antithyroid agents for approximately 6 months in an effort to induce a remission

Subclinical hypothyroidism

Basics

- TSH raised but T3, T4 normal
- no obvious symptoms

Significance

- risk of progressing to overt hypothyroidism is 2-5% per year (higher in men)
- risk increased by presence of thyroid autoantibodies

Treat if:

- TSH > 10
- thyroid autoantibodies positive
- other autoimmune disorder
- previous treatment of Graves' disease

Sulfonylureas

Sulfonylureas are oral hypoglycaemic drugs used in the management of type 2 diabetes mellitus. They work by increasing pancreatic insulin secretion and hence are only effective if functional B-cells are present. On a molecular level they bind to an ATP-dependent K^+ (K_{ATP}) channel on the cell membrane of pancreatic beta cells.

Common adverse effects

- hypoglycaemic episodes (more common with long acting preparations such as chlorpropamide)
- weight gain

Rarer adverse effects

- syndrome of inappropriate ADH secretion
- bone marrow suppression
- liver damage (cholestatic)
- peripheral neuropathy

♦Sulfonylureas should be avoided in breast feeding and pregnancy

Thiazolidinedione

◆Thiazolidinedione are a class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

◆The PPAR-gamma receptor is an intracellular nuclear receptor. It's natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have shown an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

External Links

[NICE](#)

2015 Type 2 diabetes guidelines

Thyroid cancer

Features of hyperthyroidism or hypothyroidism are not commonly seen in patients with thyroid malignancies as they rarely secrete thyroid hormones

Main points

Type	Percentage	
Papillary	70%	Often young females - excellent prognosis
Follicular	20%	
Medullary	5%	Cancer of parafollicular (C) cells, secrete calcitonin, part of MEN-2
Anaplastic	1%	Not responsive to treatment, can cause pressure symptoms
Lymphoma	Rare	Associated with Hashimoto's

Management of papillary and follicular cancer:

- total thyroidectomy
- followed by radioiodine (I-131) to kill residual cells
- yearly thyroglobulin levels to detect early recurrent disease

Further information

Type	Notes
Papillary carcinoma	• Usually contain a mixture of papillary and colloidal filled follicles • Histologically tumour has papillary projections and pale empty nuclei • Seldom encapsulated • Lymph node metastasis predominate • Haematogenous metastasis rare
Follicular adenoma	• Usually present as a solitary thyroid nodule • Malignancy can only be excluded on formal histological assessment
Follicular carcinoma	• May appear macroscopically encapsulated, microscopically capsular invasion is seen. Without this finding the lesion is a follicular adenoma. • Vascular invasion predominates • Multifocal disease rare
Medullary carcinoma	• C cells derived from neural crest and not thyroid tissue • Serum calcitonin levels often raised • Familial genetic disease accounts for up to 20% cases • Both lymphatic and haematogenous metastasis are recognised, nodal disease is associated with a very poor prognosis.
Anaplastic carcinoma	• Most common in elderly females • Local invasion is a common feature • Treatment is by resection where possible, palliation may be achieved through isthmusectomy and radiotherapy. Chemotherapy is ineffective.

External Links

[British Thyroid Association](#)

2014 Guidelines for the Management of Thyroid Cancer

Thyroid disorders: a very basic introduction

Disorders of thyroid function are very commonly encountered in clinical practice. Around 2% of the UK population has hypothyroidism (an under active thyroid gland) whilst around 1% have thyrotoxicosis (an over active gland). Both hypothyroidism and hyperthyroidism (also known as thyrotoxicosis) are around 10 times more common in women than men.

Structure and function

The thyroid gland is one of the largest endocrine organs in the body. It is a bi-lobed structure which is found in the anterior neck. As with many endocrine organs it is part of a hypothalamus-pituitary-end organ system with negative feedback cycles to maintain.

On a simple level the hypothalamus secretes thyrotropin-releasing hormone (TRH) which stimulates the anterior pituitary to secrete thyroid-stimulating hormone (TSH). This then acts on the thyroid gland increasing the production of thyroxine (T4) and triiodothyronine (T3), the two main thyroid hormones. These then act on a wide variety of tissues, helping to regulate the use of energy sources, protein synthesis, and controls the body's sensitivity to other hormones.

How are thyroid problems classified?

Hypothyroidism may be classified as follows:

- primary hypothyroidism: there is a problem with the thyroid gland itself, for example an autoimmune disorder affecting thyroid tissue (see below)
- secondary hypothyroidism: usually due to a disorder with the pituitary gland (e.g. pituitary apoplexy) or a lesion compressing the pituitary gland
- congenital hypothyroidism: due to a problem with thyroid dysgenesis or thyroid dyshormonogenesis

Whilst there are a number of causes thyrotoxicosis the vast majority are primary in nature. Congenital thyrotoxicosis is not seen and secondary hyperthyroidism is rare, account for less than 1% of cases.

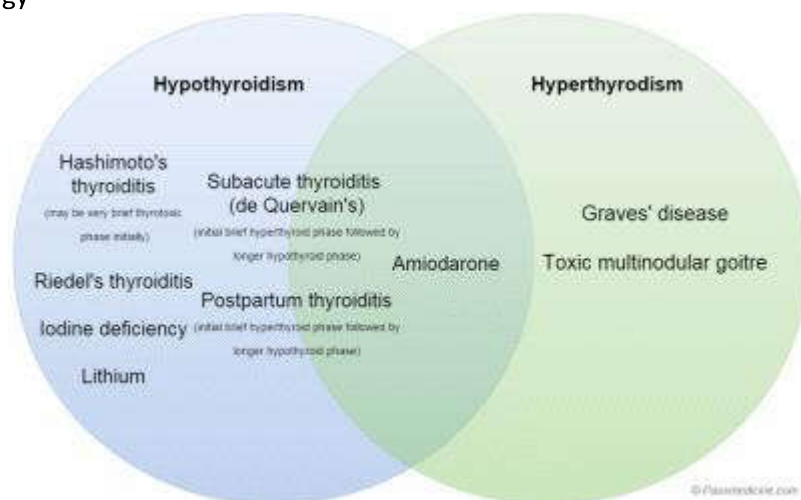
What causes thyroid problems?

The majority of thyroid problems seen in the developed world are a consequence of autoimmunity.

The table below shows the different autoimmune problems which cause thyroid dysfunction:

	Hypothyroidism	Thyrotoxicosis
Most common cause	Hashimoto's thyroiditis • most common cause • autoimmune disease, associated with type 1 diabetes mellitus, Addison's or pernicious anaemia • may cause transient thyrotoxicosis in the acute phase • 5-10 times more common in women	Graves' disease • most common cause of thyrotoxicosis • as well as typically features of thyrotoxicosis other features may be seen including thyroid eye disease
Other causes	Subacute thyroiditis (de Quervain's) • associated with a painful goitre and raised ESR Riedel thyroiditis • fibrous tissue replacing the normal thyroid parenchyma • causes a painless goitre Postpartum thyroiditis Drugs • lithium • amiodarone Iodine deficiency • the most common cause of hypothyroidism in the developing world	Toxic multinodular goitre • autonomously functioning thyroid nodules that secrete excess thyroid hormones Drugs • amiodarone

It should be remembered that a lot of the conditions mentioned above don't always cause either hypothyroidism or hyperthyroidism, there is sometimes some overlap, as shown below:



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

Symptoms and signs

Thyroid disorders can present in a large variety of ways. Often (but not always) the symptoms present are the opposite depending on whether the thyroid gland is under or over active, for example hypothyroidism may result in weight gain whilst thyrotoxicosis normally leads to weight loss

Feature	Hypothyroidism	Thyrotoxicosis
General	Weight gain Lethargy Cold intolerance	Weight loss 'Manic', restlessness Heat intolerance
Cardiac	-	Palpitations , may even provoke arrhythmias e.g. atrial fibrillation
Skin	Dry (anhidrosis), cold, yellowish skin Non-pitting oedema (e.g. hands, face) Dry, coarse scalp hair, loss of lateral aspect of eyebrows	Increased sweating Pretibial myxoedema: erythematous, oedematous lesions above the lateral malleoli Thyroid acropachy: clubbing
Gastrointestinal	Constipation	Diarrhoea
Gynaecological	Menorrhagia	Oligomenorrhea
Neurological	Decreased deep tendon reflexes Carpal tunnel syndrome	Anxiety Tremor

Investigations and diagnosis

The principle investigation is 'thyroid function tests', or TFTs for short:

- these primarily look at serum TSH and T4 levels
- T3 can be measured but is only useful clinically in a small number of cases
- remember that TSH and T4 levels will often be 'opposite' in cases of primary hypo- or hyperthyroidism. For example in hypothyroidism the T4 level is low (i.e. not enough thyroxine) but the TSH level is high, because the hypothalamus/pituitary has detected low levels of T4 and is trying to get the thyroid gland to produce more
- TSH levels are more sensitive than T4 levels for monitoring patients with existing thyroid problems and are often used to guide treatment.

The table below shows how thyroid function tests are interpreted:

Diagnosis	TSH	Free T4	Notes
Thyrotoxicosis (e.g. Graves' disease)	Low	High	
Primary hypothyroidism (e.g. Hashimoto's thyroiditis)	High	Low	
Secondary hypothyroidism	Low	Low	
Sick euthyroid syndrome	Low	Low	Common in hospital inpatients. Changes are reversible upon recovery from the systemic illness and no treatment is usually needed
Subclinical hypothyroidism	High	Normal	This is a common finding and represents patients who are 'on the way' to developing hypothyroidism but still have normal thyroxine levels. Note how the TSH levels, as mentioned above, are a more sensitive and early marker of thyroid problems
Poor compliance with thyroxine	High	Normal	Patients who are poorly compliant may only take their thyroxine in the days before a routine blood test. The thyroxine levels are hence normal but the TSH 'lags' and reflects longer term low thyroxine levels

♦A number of thyroid autoantibodies can be tested for (remember the majority of thyroid disorders are autoimmune). **The 3 main types are:**

- Anti-thyroid peroxidase (anti-TPO) antibodies
- TSH receptor antibodies
- Thyroglobulin antibodies

♦ There is significant overlap between the type of antibodies present and particular diseases, but generally speaking TSH receptor antibodies are present in around 90-100% of patients with Graves' disease and anti-TPO antibodies are seen in around 90% of patients with Hashimoto's thyroiditis

Other tests include:

- nuclear scintigraphy; toxic multinodular goitre reveals patchy uptake

Treatment

This clearly depends on the cause. For patients with hypothyroidism thyroxine is given in the form of levothyroxine to replace the underlying deficiency.

Patients with thyrotoxicosis may be treated with:

- propranolol: this is often used at the time of diagnosis to control thyrotoxic symptoms such as tremor
- carbimazole: blocks thyroid peroxidase from coupling and iodinating the tyrosine residues on thyroglobulin → reducing thyroid hormone production. Agranulocytosis is an important adverse effect to be aware of
- radioiodine treatment.

Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease.

Pathophysiology

- it is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor → retro-orbital inflammation
- the inflammation results in glycosaminoglycan and collagen deposition in the muscles

Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

Features

- the patient may be eu-, hypo- or hyperthyroid at the time of presentation
- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery.

Monitoring patients with established thyroid eye disease

For patients with established thyroid eye disease the following symptoms/signs should indicate the need for urgent review by an ophthalmologist (see EUGOGO guidelines):

- unexplained deterioration in vision
- awareness of change in intensity or quality of colour vision in one or both eyes
- history of eye suddenly 'popping out' (globe subluxation)
- obvious corneal opacity
- cornea still visible when the eyelids are closed
- disc swelling

External Links

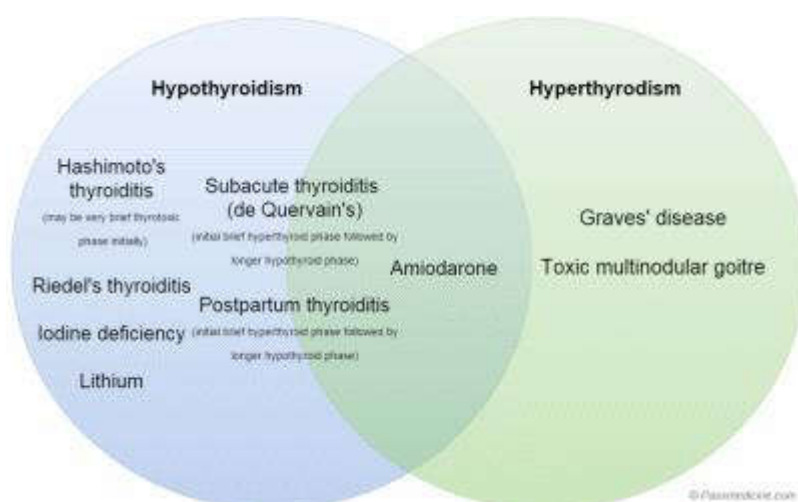
[Consensus Statement of the European Group on Graves' Orbitopathy](#)

Management of Graves' Orbitopathy

Thyroid function tests

The interpretation of thyroid function tests is usually straightforward:

Diagnosis	TSH	Free T4	Notes
Thyrotoxicosis (e.g. Graves' disease)	Low	High	In T3 thyrotoxicosis the free T4 will be normal
Primary hypothyroidism (primary atrophic hypothyroidism)	High	Low	
Secondary hypothyroidism	Low	Low	Replacement steroid therapy is required prior to thyroxine
Sick euthyroid syndrome*	Low**	Low	Common in hospital inpatients T3 is particularly low in these patients
Subclinical hypothyroidism	High	Normal	
Poor compliance with thyroxine	High	Normal	
Steroid therapy	Low	Normal	



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

*now referred to as non-thyroidal illness

**TSH may be normal in some cases.

Thyroid storm

Thyroid storm is a rare but life-threatening complication of thyrotoxicosis. It is typically seen in patients with established thyrotoxicosis and is rarely seen as the presenting feature. Iatrogenic thyroxine excess does not usually result in thyroid storm

Clinical features include:

- fever $> 38.5^{\circ}\text{C}$
- tachycardia
- confusion and agitation
- nausea and vomiting
- hypertension
- heart failure
- abnormal liver function test.

Management

- symptomatic treatment e.g. paracetamol
- treatment of underlying precipitating event
- propranolol
- anti-thyroid drugs: e.g. methimazole or propylthiouracil
- Lugol's iodine
- dexamethasone - e.g. 4mg IV qds - blocks the conversion of T4 to T3

Thyrotoxicosis

Graves' disease accounts for around 50-60% of cases of thyrotoxicosis.

Causes

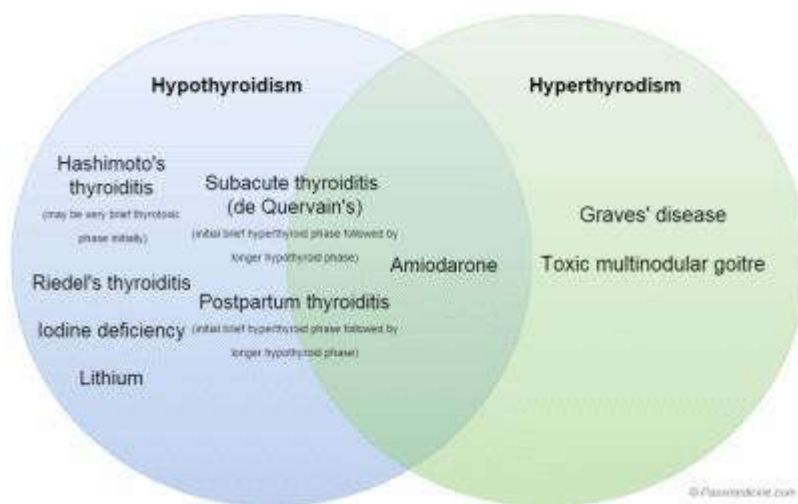
- Graves' disease
- toxic nodular goitre
- acute phase of subacute (de Quervain's) thyroiditis

Chapter : Endocrinology

- acute phase of post-partum thyroiditis
- acute phase of Hashimoto's thyroiditis (later results in hypothyroidism)
- amiodarone therapy

Investigation

- TSH down, T4 and T3 up
- thyroid autoantibodies
- other investigations are not routinely done but includes isotope scanning



Venn diagram showing how different causes of thyroid dysfunction may manifest. Note how many causes of hypothyroidism may have an initial thyrotoxic phase.

External Links

[Clinical Knowledge Summaries](#)

Hyperthyroidism guidelines

Toxic multinodular goitre

Toxic multinodular goitre describes a thyroid gland that contains a number of :

Nuclear scintigraphy reveals patchy uptake

The treatment of choice is radioiodine therapy

Water deprivation test

Method

- prevent patient drinking water
- ask patient to empty bladder
- hourly urine and plasma osmolalities

	Starting plasma osm.	Final urine osm.	Urine osm. post-DDAVP
Normal	Normal	> 600	> 600
Psychogenic polydipsia	Low	> 400	> 400
Cranial DI	High	< 300	> 600
Nephrogenic DI	High	< 300	< 300